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=> d l7
L7 HAS NO ANSWERS
L7                STR

    7 C   O
          8
    2 N
1 CH      CH 3


6 CH 5    CH
     CH     4

     Hy   CH2 NH2
   9       10  11

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT    IS MCY  UNS  AT   9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE


=> s l7 ful
FULL SEARCH INITIATED 11:11:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 403812 TO ITERATE

 99.1% PROCESSED  400000 ITERATIONS                                2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.14

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       403812 TO   403812
PROJECTED ANSWERS:               2 TO        6

L9             2 SEA SSS FUL L7

=> d 1-2

L9   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2003 ACS
RN   375848-73-0  REGISTRY
CN   Piperidine, 4-[5-(aminomethyl)-3-pyridinyl]-1-[[5-(2-phenylethyl)-3-
     pyridinyl]carbonyl]-, trihydrochloride (9CI)  (CA INDEX NAME)
MF   C25 H28 N4 O . 3 Cl H
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER
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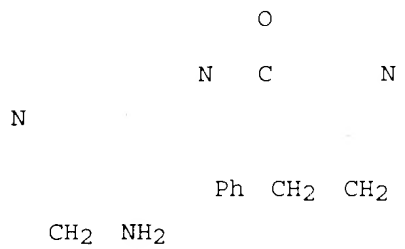
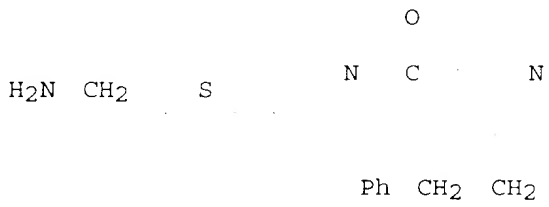


●3 HCl

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L9 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 375848-72-9 REGISTRY
CN Piperidine, 4-[5-(aminomethyl)-2-thienyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)
MF C24 H27 N3 O S . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



●2 HCl

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	153.51	153.72

FILE 'CAPLUS' ENTERED AT 11:11:51 ON 06 MAY 2003

strictly prohibited.

FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l9
L10 1 L9

=> d bib abs hitstr

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1296972	A1	20030402	EP 2001-930925	20010427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001011206	A	20030415	BR 2001-11206	20010427
	NO 2002005601	A	20030106	NO 2002-5601	20021121
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
	WO 2001-US13811	W	20010427		

OS MARPAT 136:5917
GI

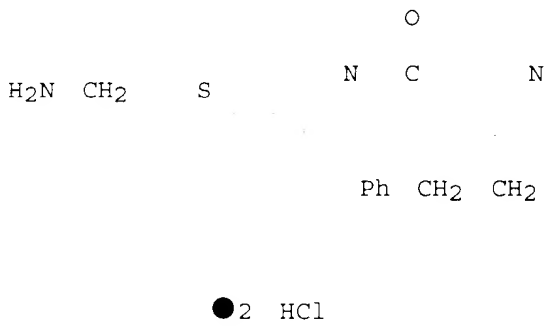
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-

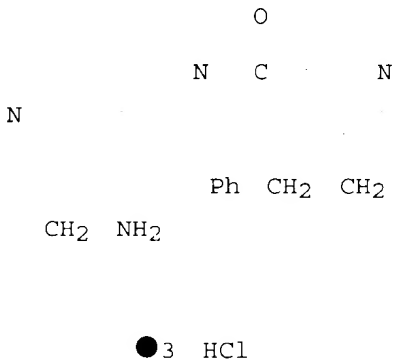
benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

IT **375848-72-9P 375848-73-0P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

RN 375848-72-9 CAPLUS
CN Piperidine, 4-[5-(aminomethyl)-2-thienyl]-1-[[5-(2-phenylethyl) 3 pyridinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)

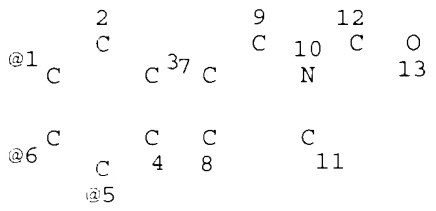


RN 375848-73-0 CAPLUS
CN Piperidine, 4-[5-(aminomethyl)-3-pyridinyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 HAS NO ANSWERS
L8 STR



VPA 14-5/6/1 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 11 4
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

=> s l8 ful
FULL SEARCH INITIATED 09:12:27 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9223 TO ITERATE

100.0% PROCESSED 9223 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L10 8 SEA SSS FUL L8

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=> s l10
L11           2 L10

=> d bib abs hitstr 1-2

L11  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS
AN   1998:126233  CAPLUS
DN   128:192644
TI   Preparation of amidinophenyl-pyrrolidines, -pyrrolines, and
     -isoxazolidines as inhibitors of factor Xa
IN   Fevig, John Matthew; Quan, Mimi Lifen
PA   Du Pont Merck Pharmaceutical Company, USA
SO   PCT Int. Appl., 206 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   WO 9806694         A1    19980219       WO 1997-US14222  19970813
         W:  AM, AU, AZ, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KG, KR, KZ, LT,
             LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, UA, VN, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     US 6057342          A     20000502       US 1997-888718   19970707
     AU 9740645          A1    19980306       AU 1997-40645    19970813
     EP 934265           A1    19990811       EP 1997-938270   19970813
     EP 934265           B1    20030102
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
     JP 2000516234       T2    20001205       JP 1998-509980   19970813
     AT 230392           E     20030115       AT 1997-938270   19970813
PRAI US 1996-689945      A     19960816
     US 1996-33436P      P     19961223
     US 1996-23417P      P     19960816
     WO 1997-US14222     W     19970813
OS   MARPAT 128:192644
GI
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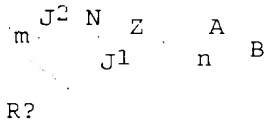


MeOCO

R?

N CH_2Ph

D I H_2N NH II

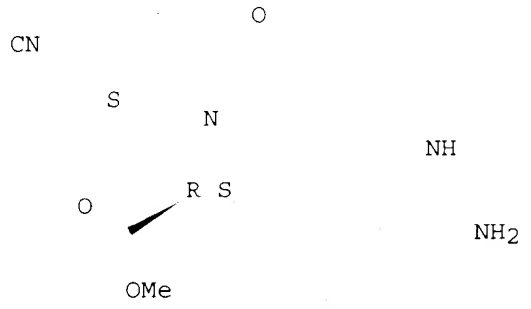
AB The title compds. [I; D, D1= CN, C(:NR7)NR8R9, NHC(:NR7)NR8R9, etc.; Z = CH2, C(O), CH2C(O), etc.; J1, J2 = O, CH2 (provided that if J1 = O, then J2 = CH2 and if J2 = O, then J1 = CH2); R = CO2R1, COR1, OR1, etc.; Ra = H, C1-4 alkyl; Rb = H; when J1, J2 = CH2, then Ra, Rb = a bond; R1 = H, (un)substituted C1-4 alkyl, C3-6 carbocyclyl, etc.; A = (un)substituted C3-13 carbocyclyl, 5-10 membered heterocyclyl; B = XY, NR2R2a, C(:NR2)NR2R2a, etc.; X = C1-4 alkylene, C(O), C(O)NR2, etc.; Y = (un)substituted C3-10 carbocyclyl, 5-10 membered heterocyclyl; R2, R2a =

H, C1-4 alkyl, Ph; R2R2a = (un)substituted 5-6 membered ring; R7 = H, OH, C1-6 alkyl, etc.; R8, R9 = H, C1-6 alkyl, (CH2)nphenyl; n = 0-3; m = 0-2] and their salts, useful as anticoagulants in treating or preventing thromboembolic disorders, were prepd. Thus, treatment of 3-cyanobenzaldehyde with Me (triphenylphosphoranylidene)acetate followed by reacting the resulting Me trans-3-cyanocinnamate with N-benzyl-N-(trimethylsilylmethyl)aminomethyl Me ether, and HCl gas bubbling through the soln. of trans-1-benzyl-3-carbomethoxy-4-(3-cyanophenyl)pyrrolidine, and treatment of the resulting solid with (NH4)2CO3 in MeOH afforded the title compd. trans-II. Some compds. I were evaluated and showed Ki of < 5 .mu.M against human thrombin.

IT **203512-01-0P 203512-02-1P 203512-09-8P**
203512-10-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amidinophenyl-pyrrolidines, -pyrrolines, and -isoxazolidines as inhibitors of factor Xa)

RN 203512-01-0 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-1-[2-[(2-cyanophenyl)thio]benzoyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

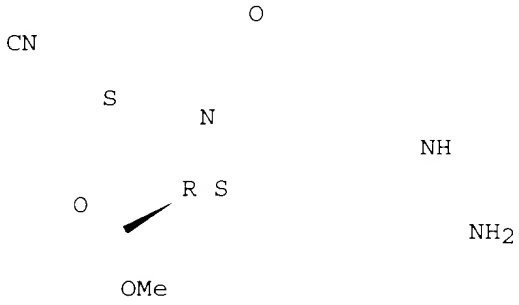


RN 203512-02-1 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-1-[2-[(2-cyanophenyl)thio]benzoyl]-, methyl ester, trans-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

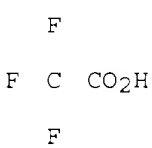
CRN 203512-01-0
CMF C27 H24 N4 O3 S

Relative stereochemistry.



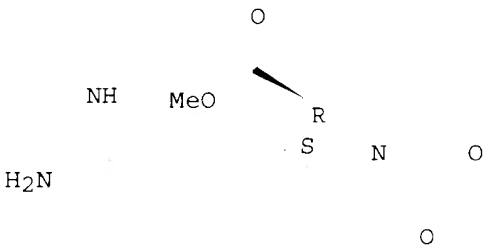
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 203512-09-8 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-, 1-(9H-fluoren-9-ylmethyl) 3-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

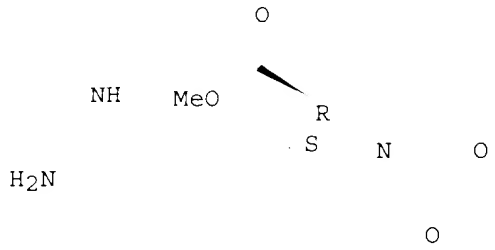


RN 203512-10-1 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-, 1-(9H-fluoren-9-ylmethyl) 3-methyl ester, trans-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

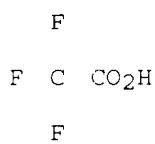
CRN 203512-09-8
CMF C28 H27 N3 O4

Relative stereochemistry.



CM 2

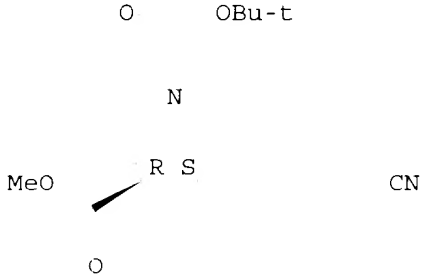
CRN 76-05-1
CMF C2 H F3 O2



IT **203512-36-1P 203512-54-3P 203512-60-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amidinophenyl-pyrrolidines, -pyrrolines, and -isoxazolidines as inhibitors of factor Xa)

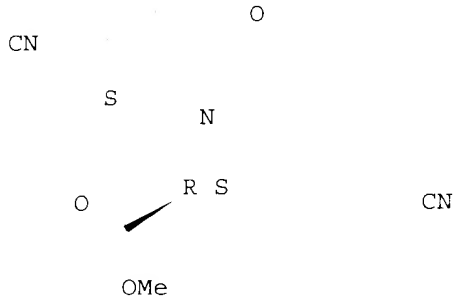
RN 203512-36-1 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(3-cyanophenyl)-, 1-(1,1-dimethylethyl) 3-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



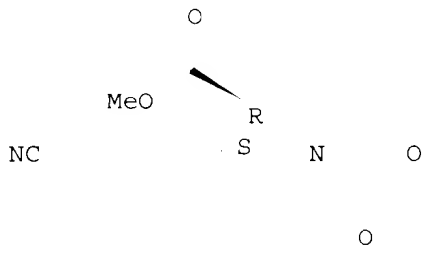
RN 203512-54-3 CAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(3-cyanophenyl)-1-[2-[(2-cyanophenyl)thio]benzoyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



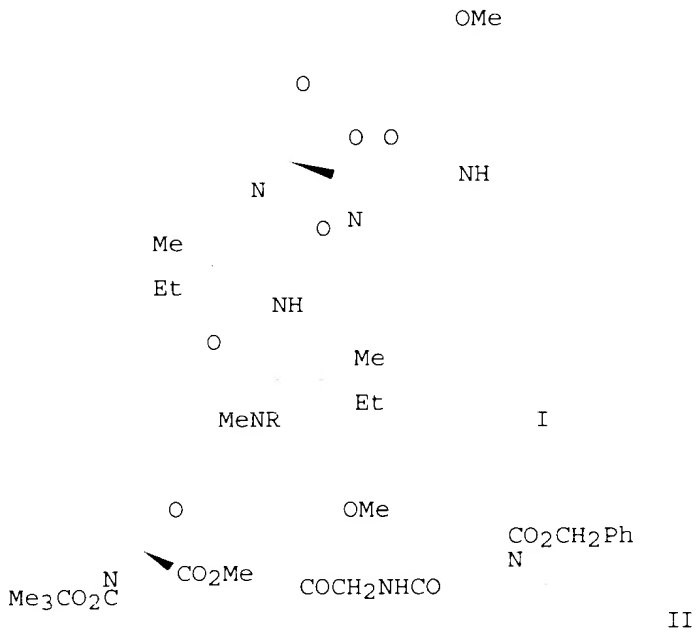
RN 203512-60-1 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(3-cyanophenyl)-, 1-(9H-fluoren-9-ylmethyl) 3-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 1982:104572 CAPLUS
DN 96:104572
TI Synthesis of peptide alkaloids. Part 4. Total synthesis of zizyphines A and B
AU Schmidt, Ulrich; Lieberknecht, Albrecht; Boekens, Hilmar; Griesser, Helmut
CS Inst. Org. Chem., Biochem. Isotopenforsch., Univ. Stuttgart, Stuttgart, D-7000/80, Fed. Rep. Ger.
SO Angewandte Chemie (1981), 93(12), 1121-2
CODEN: ANCEAD; ISSN: 0044-8249
DT Journal
LA German
GI



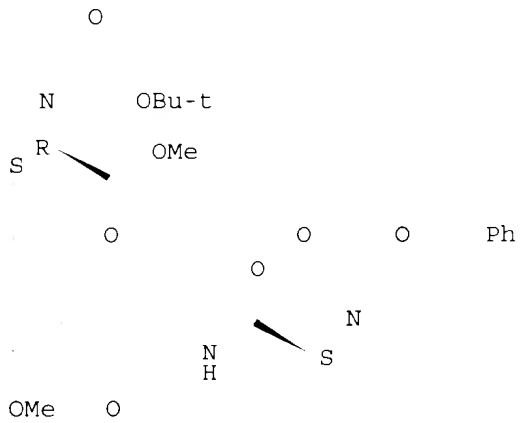
AB Zizyphine A (I, R = Me) and B (I, R = H) were prepd. by a multistep procedure from 3-bromodehydroproline Me ester and 4,3-MeO(Me3CO2C)C6Hg3ONa via intermediate II.

IT **79854-65-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

RN 79854-65-2 CAPLUS

CN 1,2-Pyrrolidinedicarboxylic acid, 3-[4-methoxy-3-[[[[1-[(phenylmethoxy)carbonyl]-2-pyrrolidinyl]carbonyl]amino]acetyl]phenyl]-, 1-(1,1-dimethylethyl) 2-methyl ester, [2R-[2.alpha.,3.beta.(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=> d his

     (FILE 'HOME' ENTERED AT 09:21:41 ON 06 MAY 2003)

     FILE 'CAPLUS' ENTERED AT 09:21:57 ON 06 MAY 2003
L1             1 S 136:5917/DN
L2           ANALYZE L1 1 RN :     592 TERMS

     FILE 'REGISTRY' ENTERED AT 09:22:35 ON 06 MAY 2003
L3           592 S L2
L4           415 S L3 AND (PIPERIDIN? OR PYRROLIDIN? OR AZEPIN?)
L5             2 S L4 AND PYRROLIDIN?
L6             0 S L4 AND AZEPIN?
L7           414 S L4 AND PIPERIDIN?

     FILE 'CAPLUS' ENTERED AT 09:24:34 ON 06 MAY 2003
L8           941 S L7

     FILE 'REGISTRY' ENTERED AT 09:24:47 ON 06 MAY 2003
L9             0 S L7 AND BAC/RL

     FILE 'CAPLUS' ENTERED AT 09:26:55 ON 06 MAY 2003
L10            1 S L8 (L) BAC/RL

     FILE 'REGISTRY' ENTERED AT 09:27:54 ON 06 MAY 2003
L11            0 S L7 AND THERAP?
L12          410 S L7 AND (PHENYL(L)PIPERIDIN?)

     FILE 'CAPLUS' ENTERED AT 09:28:52 ON 06 MAY 2003
L13          118 S L12

     FILE 'REGISTRY' ENTERED AT 09:29:15 ON 06 MAY 2003

=> s l12 and oxo?
       3235711 OXO?
L14           87 L12 AND OXO?

=> s l2 not l14


L16          505 L15 NOT L14

=> s l12 not l14
L17          323 L12 NOT L14

=> d scan

L17  323 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   Imidodicarbonic acid, [[3-[1-[[5-[[(1,1-dimethylethoxy)carbonyl][[4-
     (trifluoromethoxy)phenyl]methyl]amino]-3-pyridinyl]carbonyl]-4-
     piperidinyl]phenyl]methyl]-, bis(1,1-dimethylethyl) ester (9CI)
MF   C41 H51 F3 N4 O8
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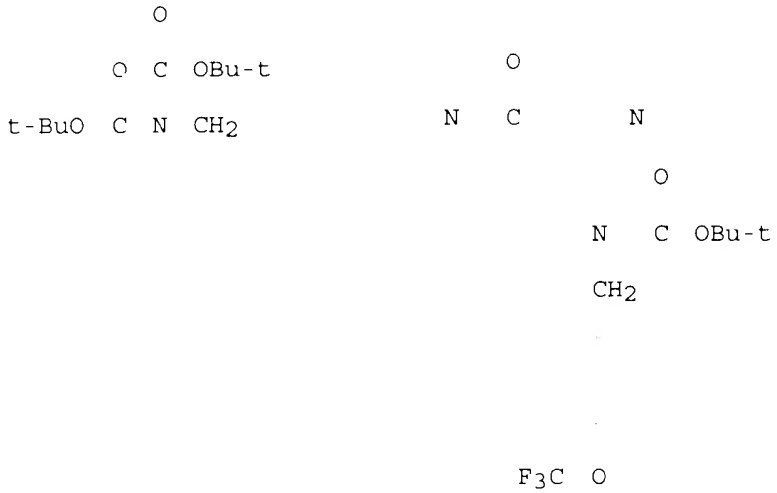

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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       4140005 AMINO
       1507059 METHYL(3W)AMINO
L18          45 L12 AND (METHYL(3W)AMINO)

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    13.46      82.91

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -1.30

FILE 'CAPLUS' ENTERED AT 09:30:30 ON 06 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l18
L19 1 L18

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	83.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.30

FILE 'REGISTRY' ENTERED AT 09:30:53 ON 06 MAY 2003

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 MAY 2003 HIGHEST RN 510776-00-8
DICTIONARY FILE UPDATES: 5 MAY 2003 HIGHEST RN 510776-00-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

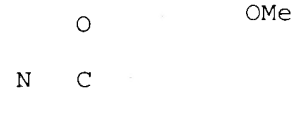
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s l17 not l18
L20 280 L17 NOT L18

=> d scan

L20 280 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN **Piperidine, 4-[3-(aminomethyl)phenyl]-1-(4-methoxybenzoyl)-, mono(trifluoroacetate) (9CI)**
MF C20 H24 N2 O2 . C2 H F3 O2

CM 1



CM 2

F

F C CO_2H

F

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l20 and aminomethyl
48240 AMINOMETHYL
L21 259 L20 AND AMINOMETHYL

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.62	87.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.30

FILE 'CAPLUS' ENTERED AT 09:31:35 ON 06 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l21
L22 1 L21

=> d bib abs

L22 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1296972	A1	20030402	EP 2001-930925	20010427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001011206	A	20030415	BR 2001-11206	20010427
	NO 2002005601	A	20030106	NO 2002-5601	20021121
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
	WO 2001-US13811	W	20010427		

OS MARPAT 136:5917
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **375847-91-9P 375847-93-1P**
RL: BSU (Biological study, unclassified); BYP (Byproduct); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

RN 375847-91-9 CAPLUS
CN Benzo[c]thiophene-1-carboxylic acid, 3-[[4-[3-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-4,5,6,7-tetrahydro-5,5-dimethyl-7-oxo-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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CRN 375847-90-8
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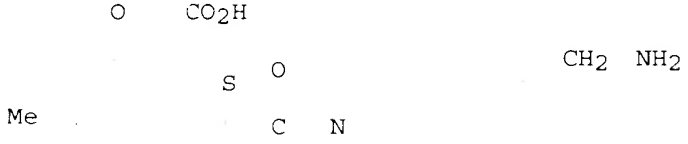

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CRN 76-05-1
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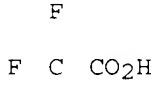
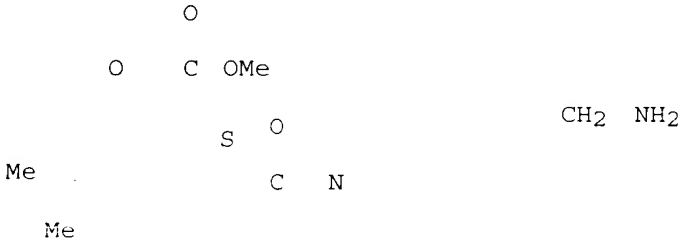


RN 375847-93-1 CAPLUS
CN Benzo[c]thiophene-1-carboxylic acid, 3-[[4-[3-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-4,5,6,7-tetrahydro-5,5-dimethyl-7-oxo-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 375847-92-0
CMF C25 H30 N2 O4 S



CM 2

CRN 76-05-1
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375846-99-4P 375847-00-0P 375847-01-1P
375847-02-2P 375847-03-3P 375847-04-4P
375847-05-5P 375847-06-6P 375847-07-7P
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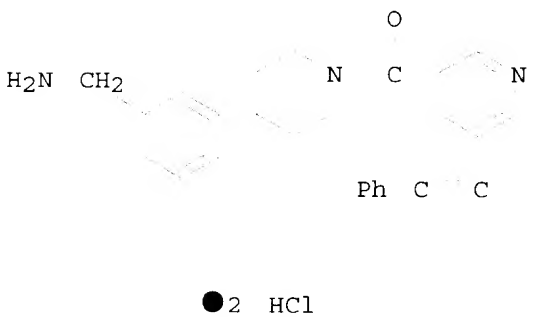
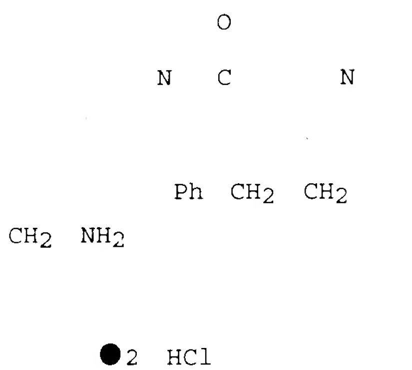
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

RN 375846-93-8 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[[5-(phenylethynyl)-3-pyridinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 375846-94-9 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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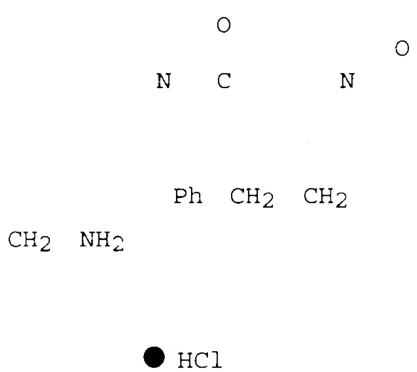
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[[1-oxido-5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 375846-96-1 CAPLUS
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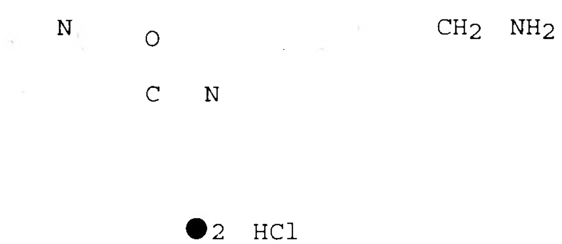
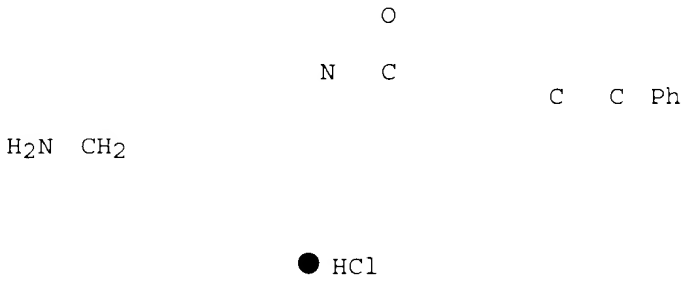


RN 375846-97-2 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[3-(phenylethynyl)benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 375846-98-3 CAPLUS
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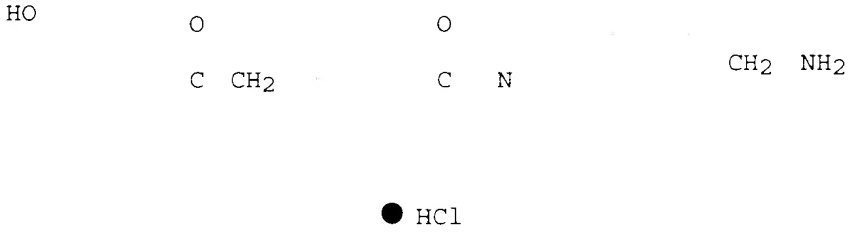

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=> s (aminomethyl(l)amidin?) and (coagul? or anticoagul?)
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         14007 AMIDIN?
            88 AMINOMETHYL(L)AMIDIN?
        122960 COAGUL?
         25286 ANTICOAGUL?
L1          27 (AMINOMETHYL(L)AMIDIN?) AND (COAGUL? OR ANTICOAGUL?)

=> s l1 and py<2000
      19718935 PY<2000
L2          16 L1 AND PY<2000

=> s l2 and us/pc
       1152526 US/PC
L3          11 L2 AND US/PC

=> d bib abs 1-11

L3   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2003 ACS
AN   2002:354079  CAPLUS
DN   136:355487
TI   Preparation of meta-benzamidine derivatives of amino acids or dipeptides
     as serine protease inhibitors
IN   Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan;
     Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary;
     Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen
     Clinton; Morgan, Phillip John
PA   UK
SO   U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S. Ser. No. 485,678.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 13
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PI   US 2002055522      A1    20020509       US 2001-988082    20011119 <--
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             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
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PRAI GB 1997-18392      A     19970829
     GB 1998-3173       A     19980213
     WO 1998-GB2605     W     19980828
     GB 1999-13823      A     19990614
     US 1999-142064P    P     19990702
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	US 2000-485678	A2	20000225
	WO 2000-GB2291	A2	20000613
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OS MARPAT 136:355487
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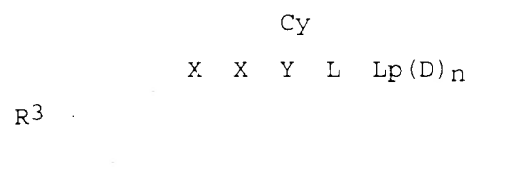

I

AB Title compds. I [R1, R2 = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R3 = R1, R2, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR1, C(R1)2, NR1 with at least one X being C, CO, CR1 or C(R1)2, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH2C(R1)2-, then R1 = H or attached to the alkylene carbon atom by a heteroatom; L = org. linker contg. 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR1; YL = cyclic group; Cy = (un)satd., (poly)cyclic, (hetero)cyclic group optionally substituted by groups R3 or Ph optionally substituted by R3; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R3; D = H bond donor group; n = 0-2], or corresponding compds. in which the (un)substituted **amidino** group R1R2NC(:NR1) is replaced with an (un)substituted **aminomethyl** group, or their physiol. tolerable salts were prepd. as serine protease inhibitors useful as antithrombotic agents. 3-**Amidino**- and 3-(**aminomethyl**)benzoyl-D-phenylglycine 4-aminomethylcyclohexylmethylamide are among 190 compds. synthesized.

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1999:69898 CAPLUS
DN 130:125409
TI Preparation of peptides as **anticoagulant** agents
IN Klimkowski, Valentine Joseph; Schacht, Aaron Leigh; Wiley, Michael Robert
PA Eli Lilly and Company, USA
SO U.S., 20 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5863929	A	19990126	US 1997-879637	19970620 <--
	US 6008367	A	19991228	US 1999-237012	19990125 <--
	US 6034104	A	20000307	US 1999-237010	19990125 <--
	US 6160176	A	20001212	US 1999-237011	19990125 <--
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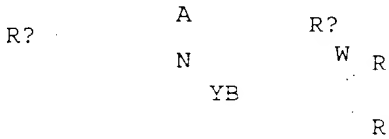
PRAI	US 1996-20371P	P	19960625		

US 1997-879637 A3 19970620
US 1999-237011 A3 19990125
OS MARPAT 130:125409
AB Peptides XCO-Y-G-R [X = 3,4-dihydroisoquinolin-1-yl or -3-yl optionally alkylated at 1, 2, and/or 3-position or corresponding hexahydro derivs. or cyclopentano- or cycloheptano analogs; Y = NRgCH2 (Rg = alkyl, cycloalkyl, (CH2)p-L-(CH2)q-T', where L is a bond, O, S, or NH; T' is alkyl, cycloalkyl, CO2H, CONH2, or aryl group; p = 0-4; q = 0-3), 1,2-azetidinediyl, 1,2-pyrrolidinediyl or derivs., 1,2-piperidinediyl; G = CONHCH2S, CH2NH(CH2)s (s = 1, 2), CH2NHCO, (CH2)tO (t = 1, 2, 3); R = 4-**amidino**-3-hydroxyphenyl group bearing 0-3 fluoro substituents] were prepd. as **anticoagulants**. Thus, N-[[4-(aminoiminomethyl)-3-hydroxyphenyl]methyl]-1-[(1R,4aR,8aR)-perhydroisoquinolin-1-ylcarbonyl]-L-prolinamide dihydrochloride was prepd. via amidation of a proline deriv. with 4-**aminomethyl**-2-hydroxybenzamide dihydrochloride.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1999:35065 CAPLUS
DN 130:110166
TI Preparation of amidinophenylpropionyltetrahydroquinolines and related compounds as antithrombotics.
IN Heckel, Armin; Soyka, Rainer; Grell, Wolfgang; Haaksma, Eric; Binder, Klaus; Zimmermann, Rainer
PA Boehringer Ingelheim Pharma K.-G., Germany
SO Ger. Offen., 50 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI DE 19727117	A1	19990107	DE 1997-19727117	19970626	<--
WO 9900371	A1	19990107	WO 1998-EP3800	19980622	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9887279	A1	19990119	AU 1998-87279	19980622	<--
EP 991624	A1	20000412	EP 1998-938621	19980622	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002511088	T2	20020409	JP 1999-505265	19980622	
MX 9911261	A	20000630	MX 1999-11261	19991206	
US 6300342	B1	20011009	US 1999-457961	19991209	<--
PRAI DE 1997-19727117	A	19970626			
WO 1998-EP3800	W	19980622			

OS MARPAT 130:110166
GI



AB Title compds. [I; Ra = H, NO2, amino, aminocarbonyl; Rb = cyano, **aminomethyl**, (substituted) **amidino**; Rc, Rd = H, F, Cl, Br, iodo, Me, MeO, NO2, amino; A = (substituted) ethylene, ethyenylene, propylene, etc.; B = bond, (substituted) methylene, ethylene, ethenylene, propylene, etc.; W = N, CH; Y = CH2, CO, CS], were prepd. Thus, 1-[3-(4-**amidinophenyl**)propionyl]-1,2,3,4-tetrahydroquinoline-6-carboxylic acid methyl-N-phenylamide (prepn. given) had a thrombin time ED200 = 0.02 .mu.M.

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1998:604913 CAPLUS
DN 129:216617
TI Preparation of amidinophenylethylbenzimidazolylcarboxamides and related compounds as thrombin inhibitors.
IN Hauel, Norbert; Ries, Uwe; Priepke, Henning; Wienen, Wolfgang; Stassen, Jean Marie
PA Boehringer Ingelheim Pharma K.-G., Germany
SO PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9837075	A1	19980827	WO 1998-EP865	19980216	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	DE 19706229	A1	19980820	DE 1997-19706229	19970218	<--
	DE 19751939	A1	19990722	DE 1997-19751939	19971124	<--
	AU 9863991	A1	19980909	AU 1998-63991	19980216	<--
	AU 742593	B2	20020110			
	EP 966454	A1	19991229	EP 1998-909468	19980216	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	EE 9900359	A	20000215	EE 1999-359	19980216	
	NZ 337323	A	20001124	NZ 1998-337323	19980216	
	JP 2001509815	T2	20010724	JP 1998-536234	19980216	
	JP 3343359	B2	20021111			
	NO 9903945	A	19991015	NO 1999-3945	19990817	<--
	US 6414008	B1	20020702	US 2000-688260	20001013	<--
PRAI	DE 1997-19706229	A	19970218			
	DE 1997-19751939	A	19971124			
	US 1997-44421P	P	19970429			
	WO 1998-EP865	W	19980216			
	US 1998-25690	A3	19980218			
	US 2000-544931	A1	20000406			

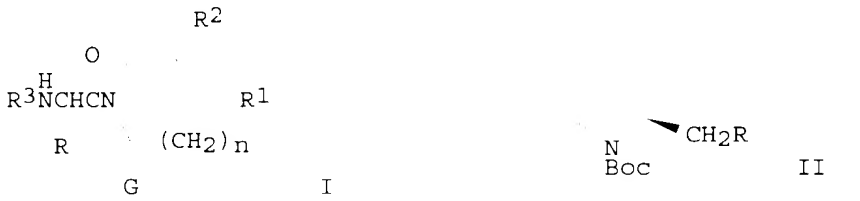
OS MARPAT 129:216617
AB Ra-A-Het-B-Ar-E [A = CO, SO2; B = CH2CH2, OCH2, SCH2, SOCH2, SO2CH2, NR1CH2; R1 = H, alkyl; E = cyano, RbNHC(:NH); Rb = H, OH, alkyl, group cleavable in vivo; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene; Het = specified bicyclic heterocyclyl; Ra = (substituted) alkyl, amino] were prepd. Thus, 1-methyl-2-[N-(4-**amidinophenyl**) **aminomethyl**]benzimidazol-5-ylcarboxylic acid N-(2-pyridyl)-N-(2-carboxyethyl)amide (prepn. given) gave a thrombin time ED200 of 0.03 .mu.M.

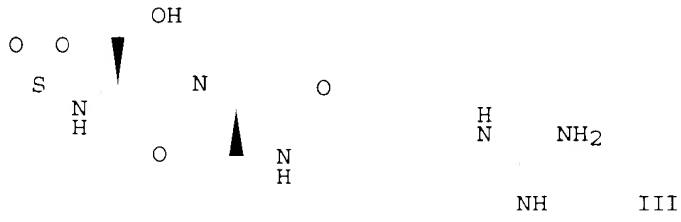
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1997:26985 CAPLUS
DN 126:104429
TI Preparation of heterocyclic peptide thrombin inhibitors
IN Kimball, Spencer D.; Das, Jagabandhu; Lau, Wan F.; Hall, Steven E.; Han, Wen Ching
PA Bristol-Myers Squibb Company, USA
SO U.S., 95 pp., Cont.-in-part of U.S. Ser. No. 146,714, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5583146	A	19961210	US 1995-373334	19950117	<--
	US 6534536	B1	20030318	US 1994-213964	19940316	<--
	CN 1109468	A	19951004	CN 1994-103732	19940331	<--
	US 5741792	A	19980421	US 1995-555560	19951108	<--
	US 5741799	A	19980421	US 1995-555561	19951108	<--
PRAI	US 1992-984640	B2	19921202			
	US 1993-56017	B2	19930503			
	US 1993-56279	B2	19930503			
	US 1993-112153	B2	19930826			
	US 1993-112155	B2	19930826			
	US 1993-146714	B2	19931110			
	US 1994-207725	B2	19940314			
	US 1994-207726	B2	19940314			
	US 1994-213964	A2	19940316			
	US 1995-373334	A3	19950117			

OS MARPAT 126:104429
GI





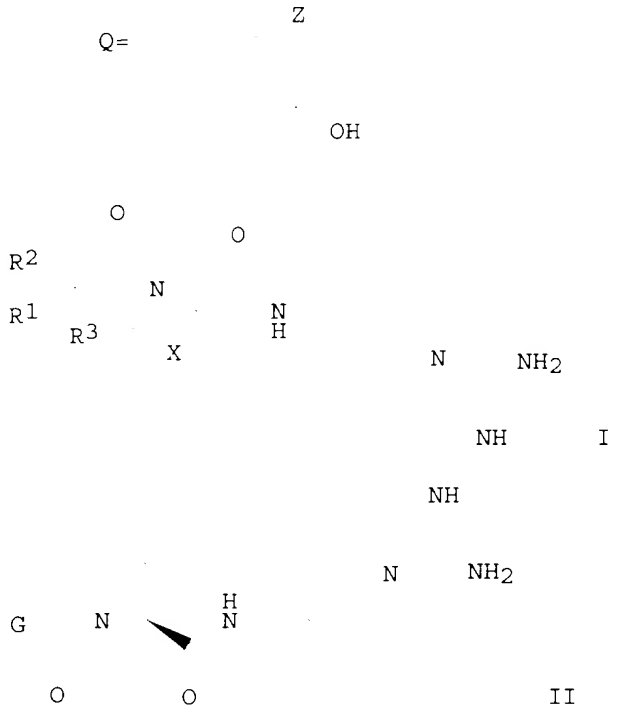
AB Heterocyclic thrombin inhibitors are provided which have the structure I [G = CONH(CH2)p-Q-A-R4, CH2-Xa-A1-R3a; R = H, hydroxyalkyl, aminoalkyl, amidoalkyl, alkyl, cycloalkyl, aryl, arylalkyl, alkenyl, alkynyl, arylalkoxyalkyl, (un)protected amino acid side chain; R1, R2 = independently H, lower alkyl, cycloalkyl, aryl, OH, alkoxy, thioalkyl,

thioaryl, amino, alkylamino; R1R2 = O, S; CR1CR2 = cycloalkyl, aryl, heteroaryl ring; R3 = H, SO2R6, COR7; R3a = guanidine, **amidine**, amino; R4 = guanidine, **amidine**, **aminomethyl**; R6 = lower alkyl, aryl, arylalkyl, heteroaryl, quinolinyl, tetrahydroquinolinyl; R7 = lower alkyl, aryl, cycloheteroalkyl, heteroaryl; n = 0-2; p = 0-5; Q = single bond, CO; A = NH, S, 4-8 membered aryl, cycloalkyl, azacycloalkyl, azaheterocycloalkyl ring, Q1; A1 = bond, C2-6 alkyl, alkenyl, alkynyl; X = CH2, O, S, NH; Xa = NH, S, S(O), SO2, O; q = 0-4; Y1, Y2 = independently H, lower alkyl, halo], including all stereoisomers and pharmaceutically acceptable salts thereof, are thus useful in inhibiting formation of thrombi (no data). Thus, substitution of protected prolinol deriv. II (Boc = Me3CO2C; R = O3SC6H4Me-4) with NaN3 gave the corresponding azide II (R = N3), which underwent catalytic hydrogenation to give amine II (R = NH2). Coupling of II (R = NH2) with HO2C(CH2)3NHZ (Z = CO2CH2Ph) gave amide II [R = NHCO(CH2)3NHZ], which was deprotected with HCl, coupled with Boc-Ser(CH2Ph)-OH, deprotected, sulfonylated with 2-naphthylsulfonyl chloride, deprotected, and guanylated with **amidinesulfonic** acid to give target compd. III.

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1996:738089 CAPLUS
DN 126:18793
TI [[(Aminoiminomethyl)piperidinyl]methyl]proline amides and related compounds useful as thrombin inhibitors
IN Vacca, Joseph P.; Lumma, William C.; Brady, Stephen F.; Tucker, Thomas Joseph
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9632110	A1	19961017	WO 1996-US4679	19960404	<--
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5629324	A	19970513	US 1995-419683	19950410	<--
	CA 2217682	AA	19961017	CA 1996-2217682	19960404	<--
	AU 9655348	A1	19961030	AU 1996-55348	19960404	<--
	AU 698705	B2	19981105			
	EP 820287	A1	19980128	EP 1996-912574	19960404	<--
	EP 820287	B1	20020327			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
	JP 11503455	T2	19990326	JP 1996-531066	19960404	<--
	AT 214928	E	20020415	AT 1996-912574	19960404	
	ES 2172657	T3	20021001	ES 1996-912574	19960404	
PRAI	US 1995-419683	A2	19950410			
	WO 1996-US4679	W	19960404			

OS MARPAT 126:18793
GI



AB Title compds. I and their pharmaceutically acceptable salts are disclosed [wherein R1, R2 = H, (un)substituted Ph, alkyl, cycloalkyl, etc.; R1R2 may form 4- to 7-membered carbocycle with 1-2 optional N,O, or S atoms; R3 = H, HO(CH2)0-4; or CR1R2R3 = tricyclic group Q (where Z = CH, O, or bond); X = (CH2)1-2, NR1CH2, SCH2]. These compds. inhibit thrombin and assocd. thrombosis. For example, L-proline Me ester HCl underwent a sequence of N-acylation with Ph2CHCH2CO2H (83%), alk. sapon. of the ester (94%), amidation with 1-(tert-butoxycarbonyl)-4-(**aminomethyl**)piperidine using EDC and HOBt (79%), acidic removal of the BOC group (100%), and guanylation of the piperidine N with **amidinesulfonic** acid, to give title compd. II [G = Ph2CHCH2]. In a test for inhibition of thrombin, the above compd. had Ki of 2.7 nM, and the similarly prepd. compd. II [G = 9-hydroxy-9-fluorenyl] had Ki of 1.1 nM.

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1996:623129 CAPLUS
DN 125:276585
TI Preparation of dipeptide amidinobenzylamides and related compounds as thrombin inhibitors.
IN Seitz, Werner; Mack, Helmut; Zierke, Thomas; Boehm, Hans-Joachim; Hoeffken, Hans Wolfgang; Koser, Stefan; Pfeiffer, Thomas; Hornberger, Wilfried
PA BASF A.-G., Germany
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9624609	A1	19960815	WO 1996-EP472	19960206 <--
	W: AU, BG, BR, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, SG, SK, TR, UA, US, AZ, BY, KG, KZ, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19504504	A1	19960814	DE 1995-19504504	19950210 <--

	DE 19506610	A1	19960829	DE 1995-19506610	19950224 <--
	AU 9647875	A1	19960827	AU 1996-47875	19960206 <--
	AU 706834	B2	19990624		
	EP 809651	A1	19971203	EP 1996-903987	19960206 <--
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	BR 9607412	A	19980707	BR 1996-7412	19960206 <--
	JP 10513462	T2	19981222	JP 1996-523967	19960206 <--
	US 5932567	A	19990803	US 1997-875515	19970730 <--
	FI 9703282	A	19970808	FI 1997-3282	19970808 <--
	NO 9703657	A	19971003	NO 1997-3657	19970808 <--
PRAI	DE 1995-19504504		19950210		
	DE 1995-19506610		19950224		
	WO 1996-EP472		19960206		

OS MARPAT 125:276585

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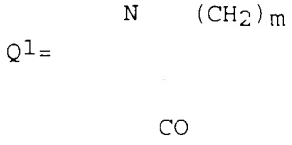

AB R1SO2ABNHDC(:NH)NH2 [R1 = OH, alkyl, fluoroalkyl, cycloalkyl, aralkyl, aryl, heteroaryl, etc.; A = NHCR4R5CO; R4 = H, alkyl, cycloalkyl, aryl, aralkyl; R5 = H, alkyl, cycloalkyl, cycloalkylmethyl, bicycloalkyl(methyl), adamantyl(methyl), etc.; B = (substituted) Q1; m = 2-4; D = (substituted) PhCH2, heteroarylmethyl], were prepd. as thrombin inhibitors (no data). Thus, BOC-Pro-OH was coupled with 4-**aminomethyl**-3-methoxybenzonitrile (prepn. given) using hydroxysuccinimide/DCC in CH2Cl2 to give 65% BOC-Proline (4-cyano-2-methoxy)benzylamide. The latter was deprotected and coupled with BOC-D-Phe(4-OMe)-OH using diisopropylethylamine/propanephosphonic anhydride to give BOC-D-(4-methoxyphenylalanyl)proline (4-cyano-2-methoxy)benzylamide. The latter was elaborated in several steps to title compd. N-methylsulfonyl-D-(4-methoxy)phenylalanylproline (2-methoxy-4-**amidino**)benzylamide acetate salt.

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1996:397160 CAPLUS
DN 125:58341
TI Preparation of naphthalene-, isoquinoline- and chroman-acetic acid derivatives as platelet aggregation inhibitors
IN Okumura, Kunio; Yokoyama, Isao; Shimazaki, Toshiyuki; Miyamoto, Michihiko; Yamashita, Hiroyuki; Kibayashi, Kenji; Yutaka, Takanori; Yazawa, Kouhei
PA Mitsui Toatsu Chemicals, Inc., Japan
SO Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 709370	A1	19960501	EP 1995-116893	19951026 <--
	EP 709370	B1	19990113		
	R: DE, FR, GB, IT				
	US 5629321	A	19970513	US 1995-544583	19951018 <--
	JP 08231486	A2	19960910	JP 1995-275433	19951024 <--
	JP 2951875	B2	19990920		
PRAI	JP 1994-264188		19941027		

OS MARPAT 125:58341

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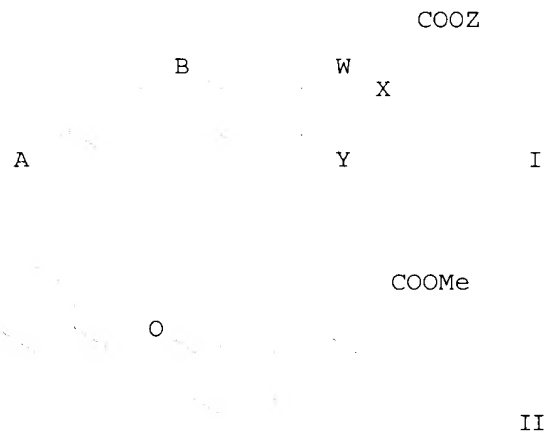

II

AB The title compds. [I; A = **amidino**, guanidino, **aminomethyl**; B = CH2O, OCH2, CH2N(R1), N(R1)CH2, CON(R1), N(R1)CO (wherein R1 = H, C1-4 alkyl); W-X = CH2CH, CH2N; CH:C; Y = CH2, O; Z = H, C1-4 alkyl], useful for prevention and therapy of thrombosis and restenosis or reocclusion after percutaneous transluminal coronary angioplasty or percutaneous transluminal coronary recanalization, were prepd. and formulated. Reaction of Me 7-hydroxy-1,2,3,4-tetrahydronaphthalene-2-acetate with 4-NCC6H4CH2Br in the presence of K2CO3 in MeCOEt followed by treatment of the intermediate II with gaseous HCl in MeOH and then addn. AcONH4 afforded I.HCl [A = **amidino**; B = CH2O; W-X = CH2CH; Y = CH2; Z = Me] which showed IC50 of 22 .mu.M against platelet aggregation in Guinea pig.

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1995:777645 CAPLUS
DN 123:169604
TI Oxazolidinone derivatives as adhesion-receptor antagonists.
IN Raddatz, Peter; Gante, Joachim; Juraszyk, Horst; Wurziger, Hanns; Pruecher, Helmut; Bernotat-Danielowski, Sabine; Melzer, Guido
PA Merck Patent G.m.b.H., Germany
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 623615	A1	19941109	EP 1994-106049	19940419	<--
	EP 623615	B1	19990630			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
	DE 4405633	A1	19941103	DE 1994-4405633	19940222	<--
	AT 181735	E	19990715	AT 1994-106049	19940419	<--
	ES 2134870	T3	19991016	ES 1994-106049	19940419	<--
	AU 9460643	A1	19941103	AU 1994-60643	19940421	<--
	AU 675698	B2	19970213			
	SK 281469	B6	20010409	SK 1994-484	19940426	
	CN 1097421	A	19950118	CN 1994-105008	19940427	<--
	CN 1052231	B	20000510			
	CZ 285761	B6	19991117	CZ 1994-1019	19940427	<--
	JP 07002847	A2	19950106	JP 1994-92058	19940428	<--

	PL 178131	B1	20000331	PL 1994-303242	19940428
	CA 2122571	AA	19941102	CA 1994-2122571	19940429 <--
	NO 9401592	A	19941102	NO 1994-1592	19940429 <--
	ZA 9402973	A	19950118	ZA 1994-2973	19940429 <--
	US 5532255	A	19960702	US 1994-234691	19940429 <--
	RU 2145961	C1	20000227	RU 1994-15184	19940429
	HU 70541	A2	19951030	HU 1994-1274	19940502 <--
PRAI	DE 1993-4314378	A	19930501		
	DE 1994-4405633	A	19940222		

OS MARPAT 123:169604

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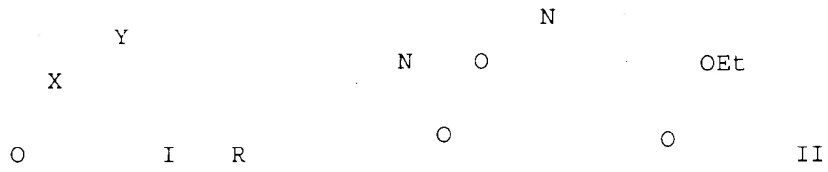


AB Title compds. I [X = O, S, NH, NA; Y = R2-bearing aziridino, azetidino, pyrrolidino, piperidino, etc., 4-(R4)-bearing piperazino, optionally substituted by OZ, SZ, NZ2, and/or carbonyloxy; Z = H, A, C1-11 acyl, Ph(CkH2k); R1 = Ph substituted by cyano, **aminomethyl**, **amidino**, guanidino, and certain other N-contg. functional groups; R2 = (CmH2m)CO2R3, (CnH2n)O(CpH2p)CO2R3; R3 = H, A, CH2Ph; R4 = H, A, CH2Ph, (CmH2m)CO2R3; A = C1-6 alkyl; k, m = 0-3; n = 0-2; p = 1-3] and salts are claimed. I are claimed useful for therapy of thrombosis, heart infarct, apoplexy, osteoporosis, inflammation, tumors, etc., and also have antimicrobial activity (no data). For example, reaction of 3-(4-cyanophenyl)-5-(methanesulfonyloxymethyl)-2-oxazolidinone [prepn. given] with 4-piperidinecarboxylic acid Et ester in MeCN in the presence of K2CO3 and KI under heating gave title compd. II (R = cyano). Sequential reaction of the latter with H2S and Et3N in pyridine, MeI in acetone, and NH4OAc in MeOH, gave II (R = **amidino**). Sapon. of this ester gave the corresponding acid, which is specifically claimed.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 1995:264625 CAPLUS

DN 122:56039

TI Substituted thiazole derivatives useful as platelet aggregation inhibitors

IN Sanfilippo, Pauline J.; Urbanski, Maud; Carson, John R.; Carmosin, Richard J.

PA McNeil-PPC, Inc., USA

SO U.S., 22 pp.
CODEN: USXXAM

DT Patent

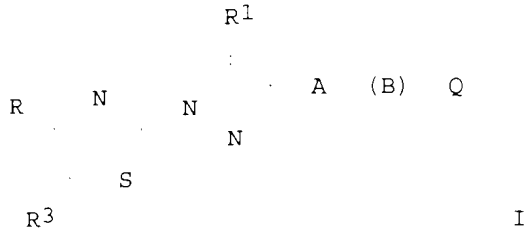
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5342851	A	19940830	US 1992-958193	19921007 <--
PRAI	US 1992-958193		19921007		

OS MARPAT 122:56039

GI



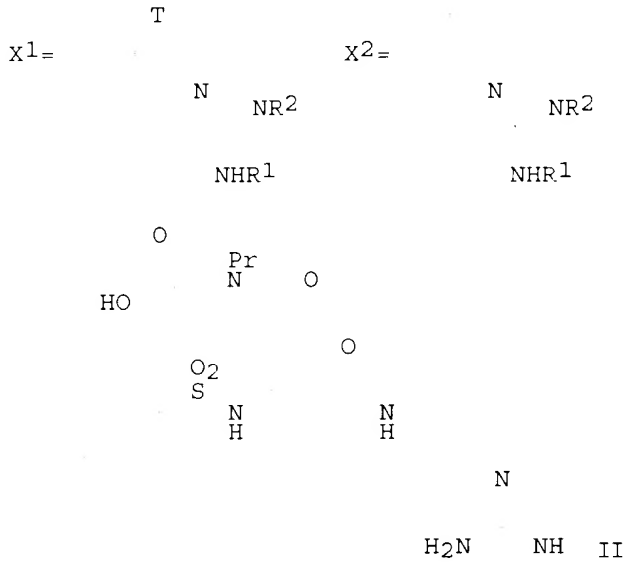
I

AB This invention relates to substituted thiazole derivs. I [R and R3 are the same or different and are selected from H, OH, CO2H, C1-4-alkylcarboxy, C1-8-alkyl, CF3, halo, (un)substituted Ph, etc.; R1 is selected from H, halo, OH, CO2H, C1-4-alkylcarboxy, C1-5-alkyl, CF3, (un)substituted Ph; R2 = H, C1-5-alkyl; A is selected from carbonyl, carboxyl, carboxamido, amido, oxymethyl, **aminomethyl**, methylene; B is selected from C1-9-alkyl, C1-9 branched alkyl, Ph, C1-5-aralkyl; Q is selected from OH, C1-5-alkoxy, halo, cyano, CO2H, C1-5-alkoxycarbonyl, NR4R5, where R4 and R5 are independently H, C1-5-alkyl, C3-8-cycloalkyl, or NR4R5 = heterocycle or guanidine, urea, thiourea, hydrazine, (un)substituted **amidine**]. These compds. are useful as inhibitors of platelet aggregation and inhibitors of adhesion mols. and may be provided in pharmaceutical compns. and in methods of treating reperfusion thrombosis injury in patients. ICx values (the concn. of the compd. in .mu.M at which the increase in light transmission = x% in drug-treated platelet conc. vs. control) were as high as x = 90 at 20 .mu.M. Formulations were given.

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1994:483062 CAPLUS
DN 121:83062
TI N-Amidinopiperidinyl-(3/4)- or N-amidino-1,4-oxazinyl-(2)-substituted sulfonamides, process for their preparation, and use as thrombin inhibitors
IN Ackermann, Jean; Banner, David; Gubernator, Klaus; Hilpert, Kurt; Schmid, Gerard
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 559046	A1	19930908	EP 1993-102767	19930222 <--
	EP 559046	B1	20010711		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2089972	AA	19930907	CA 1993-2089972	19930219 <--
	AT 203013	E	20010715	AT 1993-102767	19930222
	ES 2161217	T3	20011201	ES 1993-102767	19930222
	US 5405854	A	19950411	US 1993-21919	19930224 <--
	ZA 9301403	A	19930906	ZA 1993-1403	19930226 <--
	AU 9333916	A1	19930909	AU 1993-33916	19930301 <--
	AU 665230	B2	19951221		
	IL 120727	A1	19980816	IL 1993-120727	19930301 <--
	HU 70156	A2	19950928	HU 1993-572	19930302 <--
	RO 112863	B3	19980130	RO 1993-294	19930303 <--
	BR 9300753	A	19930908	BR 1993-753	19930304 <--
	RU 2133739	C1	19990727	RU 1993-4666	19930304 <--
	NO 9300819	A	19930907	NO 1993-819	19930305 <--
	CN 1076690	A	19930929	CN 1993-101908	19930305 <--
	JP 06025195	A2	19940201	JP 1993-69080	19930305 <--

	JP 07080848	B4	19950830		
	PL 173030	B1	19980130	PL 1993-297960	19930305 <--
	CZ 286926	B6	20000816	CZ 1993-346	19930305
	US 5578594	A	19961126	US 1994-361274	19941221 <--
	US 5677448	A	19971014	US 1996-689743	19960813 <--
	US 5763604	A	19980609	US 1997-869558	19970604 <--
	FI 9901361	A	19990614	FI 1999-1361	19990614 <--
PRAI	CH 1992-728	A	19920306		
	CH 1993-180	A	19930121		
	US 1993-21919	A3	19930224		
	IL 1993-104893	A3	19930301		
	FI 1993-990	A3	19930305		
	US 1994-361274	A3	19941221		
	US 1996-689743	A3	19960813		
OS	MARPAT 121:83062				
GI					

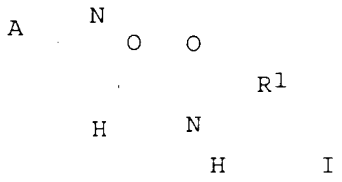


AB Title compds. ASO2N(Y)MCON(Q)CH2X [I; X = oxazinyl and piperidinyl groups X1 or X2; T = CH2 or O; R1, R2 = H, alkoxycarbonyl; Y = H and in some cases CH2CO2H or SO2A'; A, A' = (hetero)aryl, (cyclo)alkyl, heterocyclyl; Q = H, certain (un)substituted alkyl; M = CH(Z), CH(Z)CH2; Z = various pendant groups, mostly contg. amide functions] were prepd. as drugs, primarily as inhibitors of thrombin-induced platelet aggregation and fibrinogen **coagulation**. For example, condensation of (S)-1-**amidino**-3-(**aminomethyl**)piperidine-2HCl with the corresponding acid by the BOP method gave (S)-[N-allyl-[3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-(2-naphthylsulfonylamino)propionyl]amino]acetic acid Et ester hydrochloride, which underwent hydrolysis by aq. NaOH and hydrogenation over Pd/C to give title compd. (S)-[[3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-(2-naphthylsulfonylamino)propionyl]propylamino]acetic acid (II). I showed high specificity for inhibition of thrombin over other serine proteases, with II having Ki = 0.22 and 4300 nM for thrombin and trypsin, resp. (ratio = 19,545). Approx. 200 I were prepd. in 73 synthetic examples.

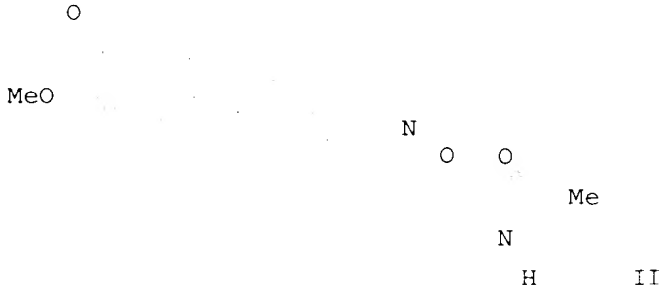
AN 1998:147317 CAPLUS
DN 128:192646
TI Preparation of isoxazolines as antimicrobials
IN Barbachyn, Michael R.; Thomas, Richard C.; Cleek, Gary J.
PA Pharmacia & Upjohn Company, USA; Barbachyn, Michael R.; Thomas, Richard C.; Cleek, Gary J.
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9807708	A1	19980226	WO 1997-US13934	19970815
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739736	A1	19980306	AU 1997-39736	19970815
	EP 920421	A1	19990609	EP 1997-937156	19970815
	EP 920421	B1	20021106		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 5990136	A	19991123	US 1997-999753	19970815
	JP 2000516245	T2	20001205	JP 1998-510781	19970815
	AT 227277	E	20021115	AT 1997-937156	19970815
	US 6093736	A	20000725	US 1999-386647	19990831
PRAI	US 1996-24287P	P	19960821		
	US 1997-999753	A3	19970815		
	WO 1997-US13934	W	19970815		

OS MARPAT 128:192646
GI



I



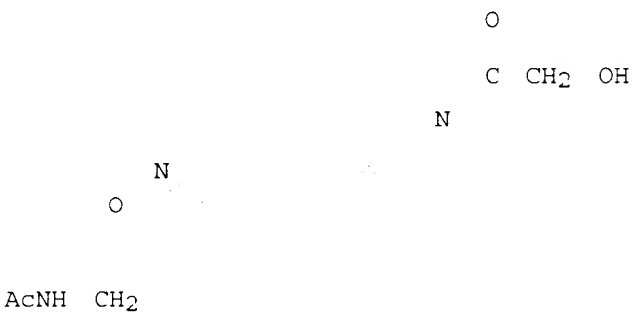
II

AB The title compds. [I; R1 = H, (un)substituted C1-8 alkyl, C3-6 cycloalkyl,

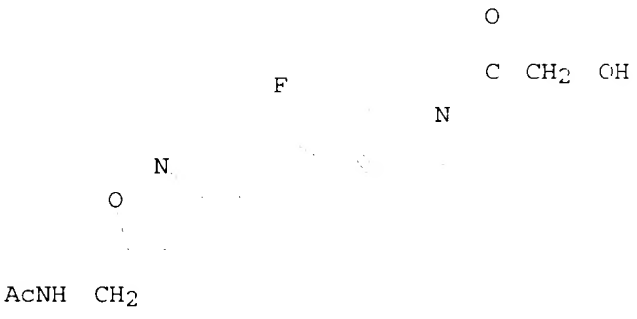
etc.; A = substituted Ph, 5-6 membered heteroaryl, .beta.-carbolinyl, etc.], useful as antimicrobial agents, were prepd. Thus, cyclization of 4-bromo-N-hydroxybenzenecarboximidoyl chloride with allyl alc. followed by methanesulfonylation of the resulting 4,5-dihydro-3-(4-bromophenyl)-5-(hydroxymethyl)isoxazole, treatment of 4,5-dihydro-3-(4-bromophenyl)-5-(methanesulfonyloxymethyl)isoxazole with NH4OH, acetylation of 4,5-dihydro-3-(4-bromophenyl)-5-(aminomethyl)isoxazole with Ac2O, and reaction of N-{[4,5-dihydro-3-(4-bromophenyl)-5-isoxazolyl]methyl}acetamide with 2-methoxy-5-trimethylstannyltropone afforded the title compd. II which showed, e.g., MIC of 4 .mu.g/mL against Staphylococcus aureus UC No. 9213.

IT **203634-03-1P 203634-06-4P 203634-09-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of isoxazolines as antimicrobials)

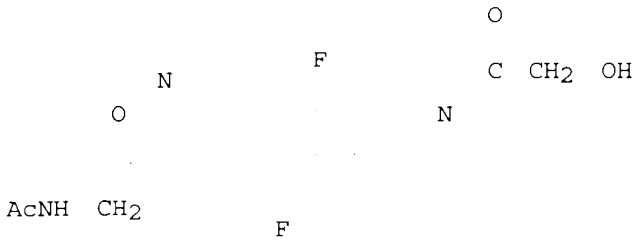
RN 203634-03-1 CAPLUS
CN Acetamide, N-[[4,5-dihydro-3-[4-[2,3,6,7-tetrahydro-1-(hydroxyacetyl)-1H-azepin-4-yl]phenyl]-5-isoxazolyl]methyl]- (9CI) (CA INDEX NAME)



RN 203634-06-4 CAPLUS
CN Acetamide, N-[[3-[3-fluoro-4-[2,3,6,7-tetrahydro-1-(hydroxyacetyl)-1H-azepin-4-yl]phenyl]-4,5-dihydro-5-isoxazolyl]methyl]- (9CI) (CA INDEX NAME)



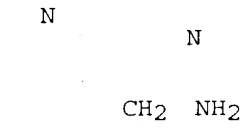
RN 203634-09-7 CAPLUS
CN Acetamide, N-[[3-[3,5-difluoro-4-[2,3,6,7-tetrahydro-1-(hydroxyacetyl)-1H-azepin-4-yl]phenyl]-4,5-dihydro-5-isoxazolyl]methyl]- (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1989:186396 CAPLUS
DN 110:186396
TI Mast cell tryptase and chymase reverse airway smooth muscle relaxation induced by vasoactive intestinal peptide in the ferret
AU Franconi, Giovanna M.; Graf, Paul D.; Lazarus, Stephen C.; Nadel, Jay A.; Caughey, George H.
CS Cardiovasc. Res. Inst., Univ. California, San Francisco, CA, 94143, USA
SO J. Pharmacol. Exp. Ther. (1989), 248(3), 947-51
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
AB To explore the potential role of mast cell mediators in modulating neural control of airway tone, the effect of the mast cell proteases **tryptase** and chymase on airway smooth muscle relaxation induced by VIP was studied in the ferret airway. Tracheal rings precontracted by serotonin (10-6M) in a muscle bath were relaxed by VIP (10-7M). Protease-rich supernatant obtained by degranulation of dog mastocytoma cells reversed VIP-induced relaxation, as did highly purified **tryptase** and chymase incubated with the tracheal rings. Either enzyme completely reversed the effect of VIP, but **tryptase** was more potent than chymase, paralleling previous test tube observations on the relative rates of VIP cleavage by the two enzymes. Inhibitors of mast cell **tryptase** and chymase preincubated with the supernatant or with the purified proteases prevented reversal of VIP-induced relaxation. Mast cell proteases did not reverse the tracheal relaxation caused by the nonpeptide **adrenergic** agonist isoproterenol. Thus, the mast cell proteases **tryptase** and chymase counteract the smooth muscle relaxant effects of VIP in ferret trachea and suggest a potential role for the mast cell proteases in the modulation of nonadrenergic neural control of airway tone by VIP.

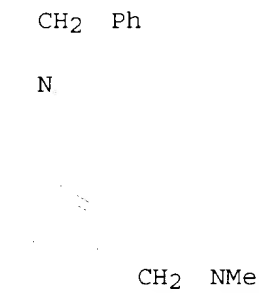
L5 ANSWER 1 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-49-5** REGISTRY
CN **3-Pyridinemethanamine, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C17 H21 N3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

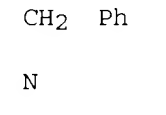
L5 ANSWER 2 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-43-9** REGISTRY
CN **Benzenemethanamine, N,N-dimethyl-3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C20 H26 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

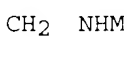


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 3 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-40-6** REGISTRY
CN **Benzenemethanamine, N-methyl-3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C19 H24 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

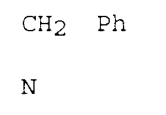


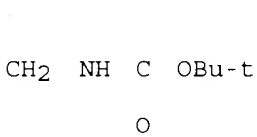


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 4 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-36-0** REGISTRY
CN **Carbamic acid, [[4-[1-(phenylmethyl)-3-pyrrolidinyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C23 H30 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 5 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-35-9** REGISTRY
CN **Carbamic acid, [[3-[1-(phenylmethyl)-3-pyrrolidinyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI)** (CA INDEX NAME)
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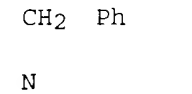
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



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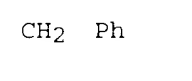
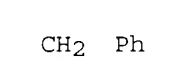
1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 6 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-34-8** REGISTRY
CN **Pyrrolidine, 1-(phenylmethyl)-3-[4-(phenylmethyl)phenyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C24 H25 N
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 7 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-33-7** REGISTRY
CN **Benzenemethanamine, 3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
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MF C18 H22 N2
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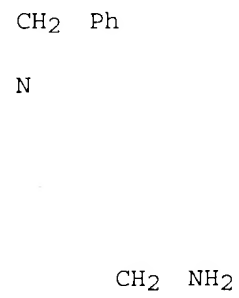
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 8 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-32-6** REGISTRY
CN **3-Pyridinecarbonitrile, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
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MF C17 H17 N3
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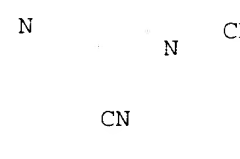
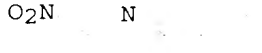
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 9 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **150281-31-5** REGISTRY
CN **Pyridine, 2-nitro-6-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C16 H17 N3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

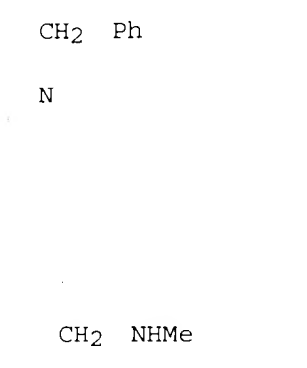


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 10 OF 16 REGISTRY COPYRIGHT 2003 ACS

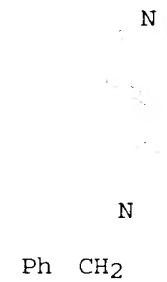
RN **150281-30-4** REGISTRY
CN **Benzenemethanamine, N-methyl-4-[1-(phenylmethyl)-3-pyrrolidinyl]-(9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C19 H24 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 11 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **145105-06-2** REGISTRY
CN **Pyridine, 4-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C16 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

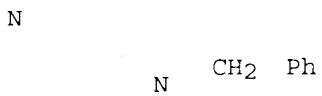


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **145105-05-1** REGISTRY
CN **Pyridine, 3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD

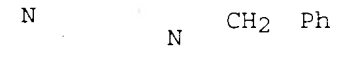
MF C16 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 13 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **145105-04-0** REGISTRY
CN **Pyridine, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C16 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 14 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **145105-03-9** REGISTRY
CN **Benzonitrile, 4-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **4-[1-(Phenylmethyl)-3-pyrrolidinyl]benzonitrile**
FS 3D CONCORD
MF C18 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

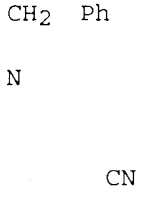
2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 15 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **145105-02-8** REGISTRY
CN **Benzonitrile, 3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **3-[1-(Phenylmethyl)-3-pyrrolidinyl]benzonitrile**
FS 3D CONCORD
MF C18 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 16 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN **145105-01-7** REGISTRY
CN **Benzonitrile, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C18 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



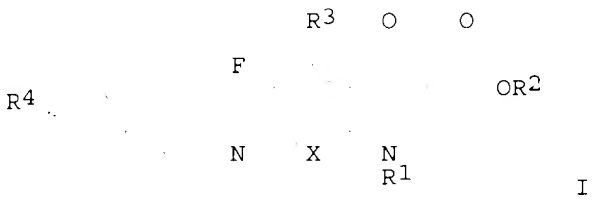
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

AN 1993:580755 CAPLUS
DN 119:180755
TI Preparation of 7-substituted quinolones and naphthyridones as antibacterial agents
IN Laborde, Edgardo; Schroeder, Mel
PA Warner-Lambert Co., USA
SO U.S., 17 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5221676	A	19930622	US 1992-832188	19920206
	WO 9316077	A1	19930819	WO 1993-US266	19930112
	W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PT, RU, SK				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9334701	A1	19930903	AU 1993-34701	19930112
	ZA 9300826	A	19940805	ZA 1993-826	19930205
	US 5342844	A	19940830	US 1993-14286	19930205
	US 5384407	A	19950124	US 1994-221145	19940330
	US 5446044	A	19950829	US 1994-312598	19940927
	US 5622966	A	19970422	US 1995-450090	19950525
PRAI	US 1992-832188		19920206		
	WO 1993-US266		19930112		
	US 1993-14286		19930205		
	US 1994-221145		19940330		
	US 1994-312598		19940927		

OS MARPAT 119:180755
GI

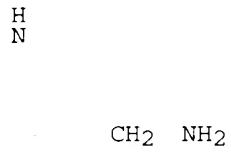


I

AB Title compds. I (X = HC, FC, ClC, MeOC, F3CC, N; R1 = (substituted) C1-4 alkyl, -C3-6 cycloalkyl, -Ph; R2 = H, C1-4 alkyl, cation; R3 = H, H2N, Me; R4 = (substituted) methylamino), salt or quaternary ammonium salt thereof, are prepd. 7-Chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid, 2-(3-pyrrolidinyl)benzenemethanamine (prepn. given) and EtN(CHMe2)2 in MeCN were refluxed for 24 h to give after recrystn. I (R1 = cyclopropyl, R2 = R3 = H, R4 = 2-H2NCH2, X = N) (II). II showed a min. inhibitory concn. of 0.05 .mu.g/mL against Streptococcus faecalis.

IT **150281-37-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of antibacterials)

RN 150281-37-1 CAPLUS
CN Benzenemethanamine, 2-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)



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=> s tryptase(l)inhibit?
          1244 TRYPTASE
       1503214 INHIBIT?
L1          515 TRYPTASE(L)INHIBIT?

=> s l1(L)(piperidin? or pyrrolidin?)
         72627 PIPERIDIN?
         44076 PYRROLIDIN?
L2           16 L1(L)(PIPERIDIN? OR PYRROLIDIN?)

=> d bib abs 1-16

L2   ANSWER 1 OF 16  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:594841  CAPLUS
TI   Preparation of N,N'-bis(N-alkanoyl-2-alkoxycarbonyl-4-pyrrolidinyl
     )-2,6-dioxoperhydro-1,5-diazocine-1,5-diacetamides and analogs as
     tryptase inhibitors
IN   Baer, Thomas; Martin, Thomas; Stadlwieser, Josef; Wollin, Stefan-Lutz;
     Zech, Karl; Sommerhoff, Christian P.; Ulrich, Wolf-Ruediger
PA   BYK Gulden Lomberg Chemische Fabrik Gmbh, Germany
SO   PCT Int. Appl., 28 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2002060895      A1   20020808       WO 2002-EP200831 20020126
         W:  AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR,
             HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL,
             RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
PRAI EP 2001-102098    A    20010131
GI
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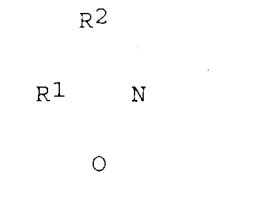

```
AB   Z(CH2CCONHR)2 [I; R = pyrrolidinyl group II; R1 = H2NCH2Z1Z2; R2
     = CO2R3 or CONHR5; R3 = H, alkyl, CH2Ph; R5 = H or cyclopropyl; Z =
     2,6-dioxoperhydro-1,5-diazocine-1,5-diyl; Z1 = 1,4-phenylene or
     -cyclohexylene; Z2 = bond or CH2CH2] were prepd. as tryptase
     inhibitors (no data).  Thus, 4-(OOHC)C6H4CH:CHCO2Me was converted
     in 3 steps to 4-(BocHNH2C)C6H4CH2CH2CO2H which was amidated by Me
     4-azidoprolinate and the reduced product amidated by Z(CH2CO2H)2 (prepn.
     given) to give I [R1 = CH2CH2C6H4(CH2NH2)-4, R2 = CO2Me].
RE.CNT  2     THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2   ANSWER 2 OF 16  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:465859  CAPLUS
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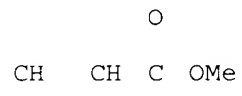
(97501-93-4/RN)

L2 36 (103565-40-8/BI OR 132691-45-3/BI OR 162046-58-4/BI OR 325470-40-4/BI OR 325470-41-5/BI OR 325470-45-9/BI OR 444899-38-1/BI OR 444899-40-5/BI OR 444899-42-7/BI OR 444899-44-9/BI OR 444899-46-1/BI OR 444899-49-4/BI OR 444899-53-0/BI OR 444899-55-2/BI OR 444899-60-9/BI OR 444899-62-1/BI OR 444899-64-3/BI OR 444899-66-5/BI OR 444899-68-7/BI OR 444899-70-1/BI OR 444899-72-3/BI OR 444899-74-5/BI OR 444899-76-7/BI OR 444899-78-9/BI OR 444899-80-3/BI OR 444899-84-7/BI OR 444899-85-8/BI OR 445304-16-5/BI OR 445304-17-6/BI OR 445304-18-7/BI OR 445304-19-8/BI OR 5292-43-3/BI OR 7560-50-1/BI OR 84520-69-4/BI OR 935-18-2/BI OR 97501-93-4/BI)

=> d scan

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Propenoic acid, 3-[4-[(hydroxyimino)methyl]phenyl]-, methyl ester (9CI)
MF C11 H11 N O3

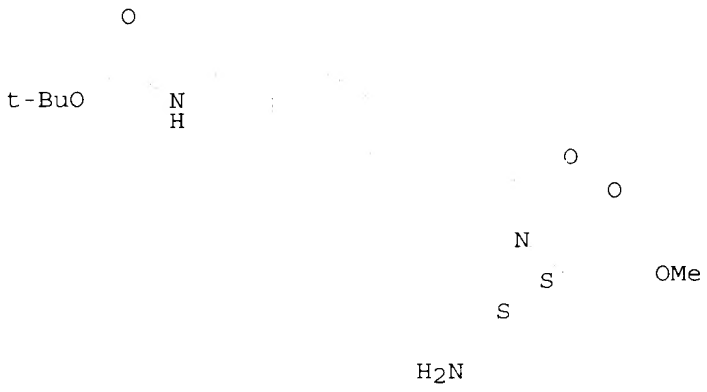


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-amino-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, methyl ester, (4S)- (9CI)
MF C21 H31 N3 O5

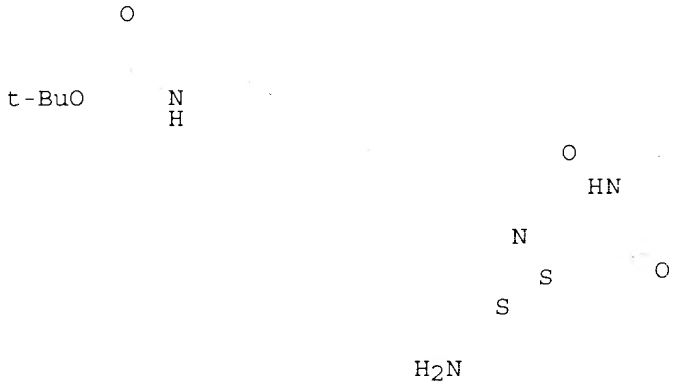
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Carbamic acid, [[4-[3-[(2S,4S)-4-amino-2-[(cyclopropylamino)carbonyl]-1-pyrrolidinyl]-3-oxopropyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI)
MF C23 H34 N4 O4

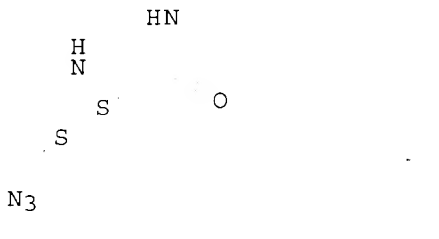
Absolute stereochemistry.



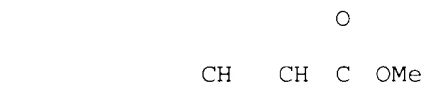
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyrrolidinecarboxamide, 4-azido-N-cyclopropyl-, (2S,4S)- (9CI)
MF C8 H13 N5 O

Absolute stereochemistry.



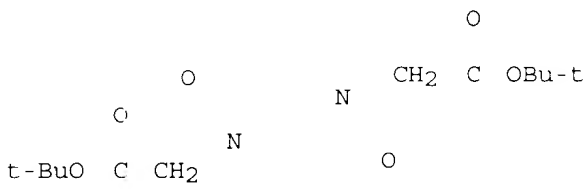
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Propenoic acid, 3-(4-formylphenyl)-, methyl ester (9CI)
MF C11 H10 O3



OHC

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-1,5(2H,6H)-diacetic acid, tetrahydro-2,6-dioxo-, bis(1,1-dimethylethyl) ester (9CI)
MF C18 H30 N2 O6

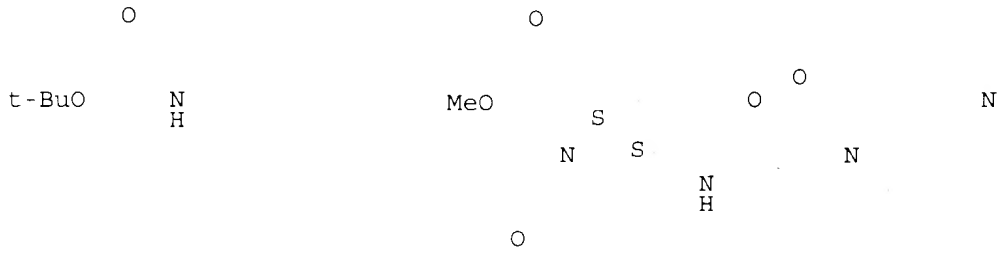


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

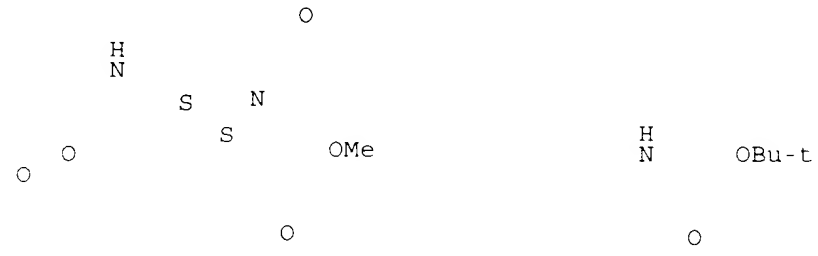
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C52 H72 N8 O14

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

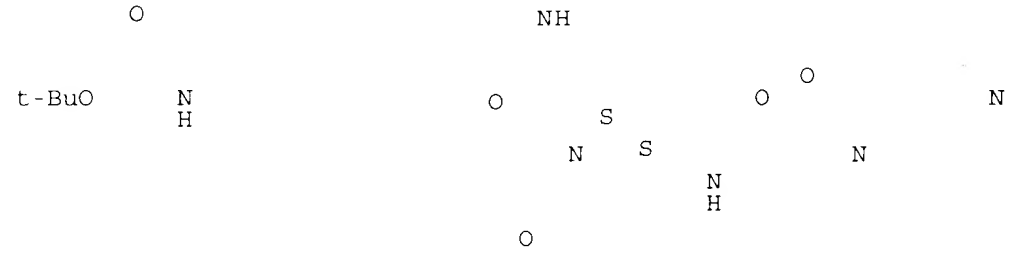


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C56 H78 N10 O12

Absolute stereochemistry.

PAGE 1-A



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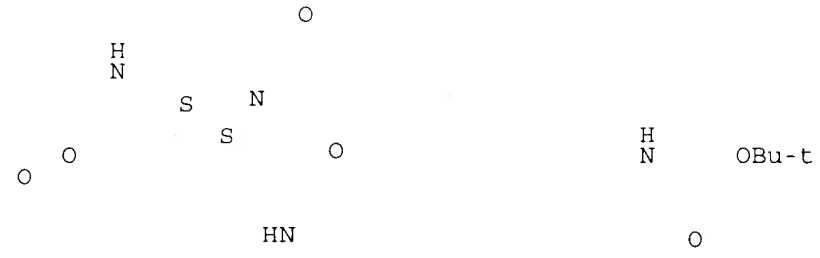
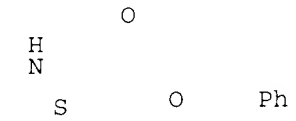


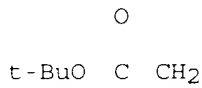
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-, phenylmethyl ester, (4S)- (9CI)
MF C12 H14 N4 O2

Absolute stereochemistry.

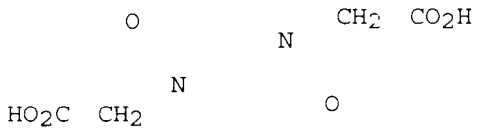


L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Acetic acid, bromo-, 1,1-dimethylethyl ester (9CI)
MF C6 H11 Br O2
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-1,5(2H,6H)-diacetic acid, tetrahydro-2,6-dioxo- (9CI)
MF C10 H14 N2 O6



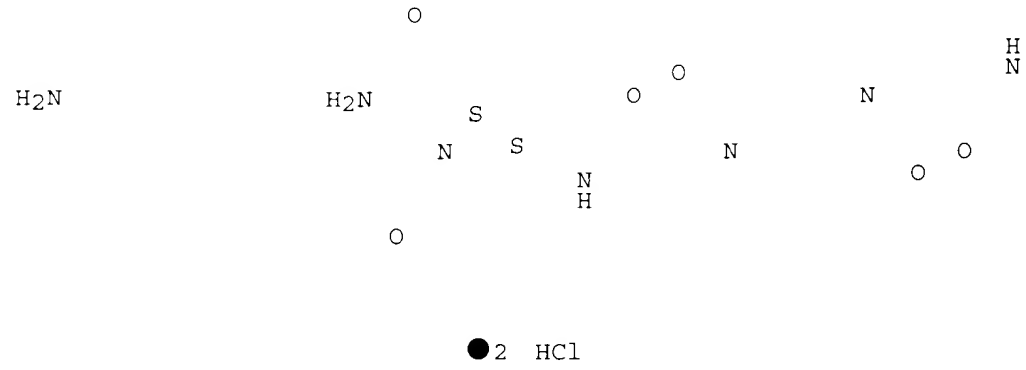
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-1,5(2H,6H)-diacetamide, N,N'-bis[(3S,5S)-5-(aminocarbonyl)-1-[3-[4-(aminomethyl)phenyl]-1-oxopropyl]-3-pyrrolidinyl]tetrahydro-2,6-dioxo-, dihydrochloride (9CI)
MF C40 H54 N10 O8 . 2 Cl H

Absolute stereochemistry.

PAGE 1-A



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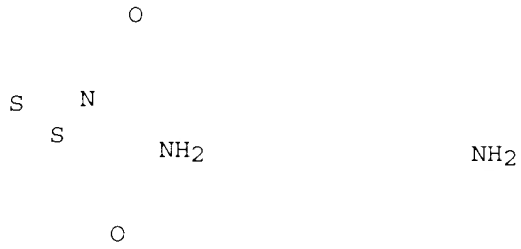
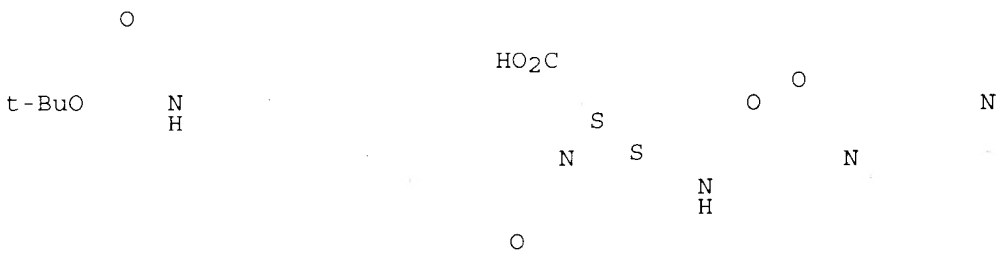


L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C50 H68 N8 O14

Absolute stereochemistry.

PAGE 1-A



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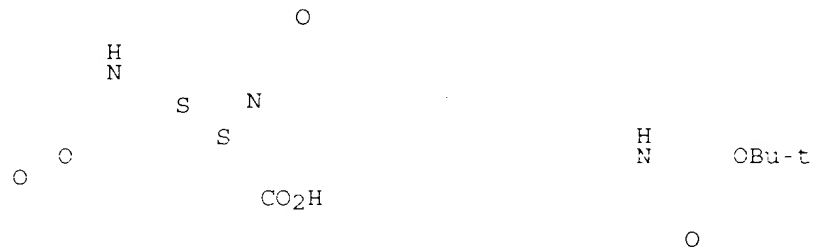
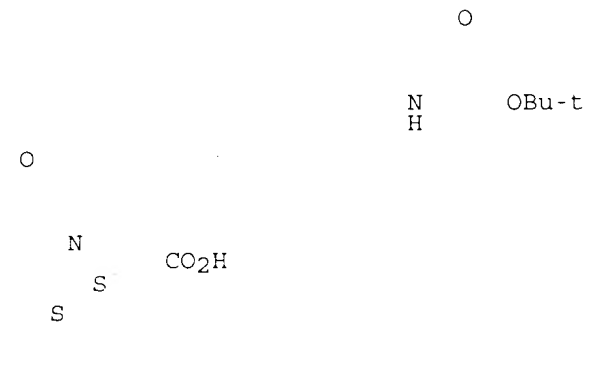


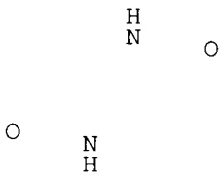
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, (4S)- (9CI)
MF C20 H27 N5 O5

Absolute stereochemistry.

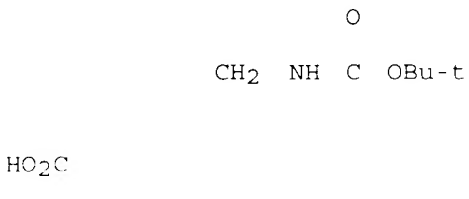


L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-2,6(1H,3H)-dione, tetrahydro- (6CI, 7CI, 8CI, 9CI)
MF C6 H10 N2 O2
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Cyclohexanecarboxylic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]- (9CI)
MF C13 H23 N O4

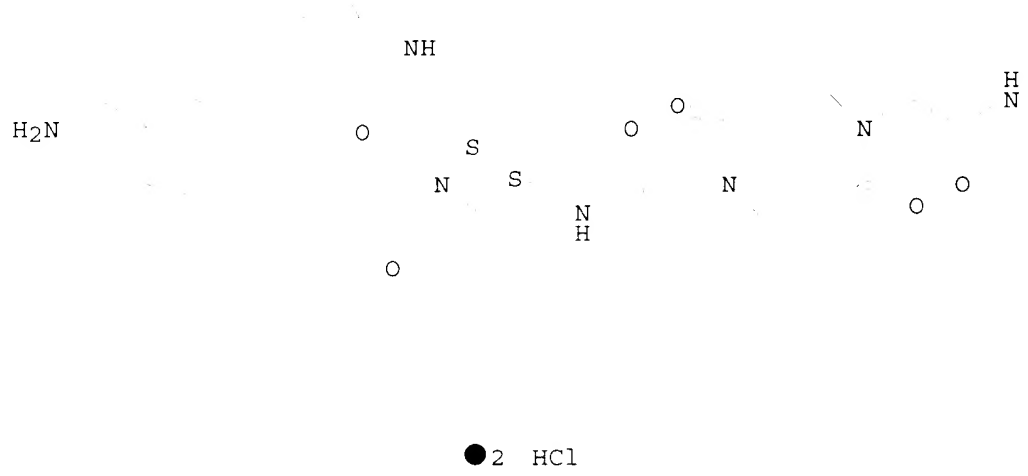


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-1,5(2H,6H)-diacetamide, N,N'-bis[(3S,5S)-1-[3-[4-(aminomethyl)phenyl]-1-oxopropyl]-5-[(cyclopropylamino)carbonyl]-3-pyrrolidinyl]tetrahydro-2,6-dioxo-, dihydrochloride (9CI)
MF C46 H62 N10 O8 . 2 Cl H

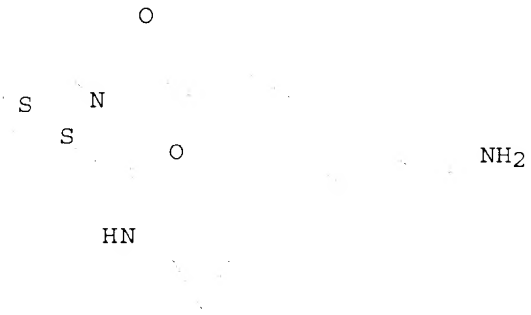
Absolute stereochemistry.

PAGE 1-A



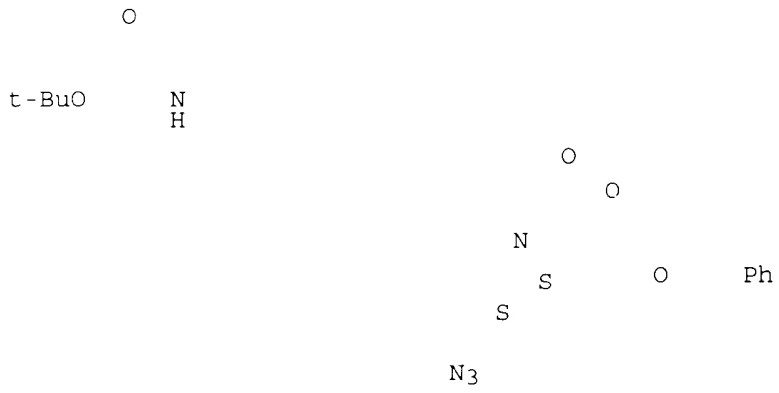
● 2 HCl

PAGE 1-B



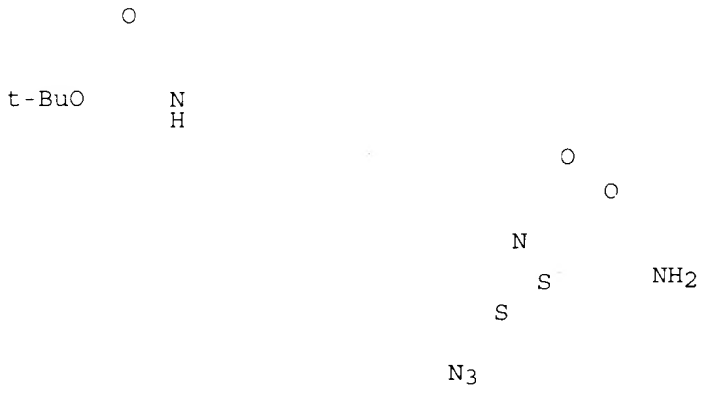
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, phenylmethyl ester, (4S)- (9CI)
MF C27 H33 N5 O5

Absolute stereochemistry.



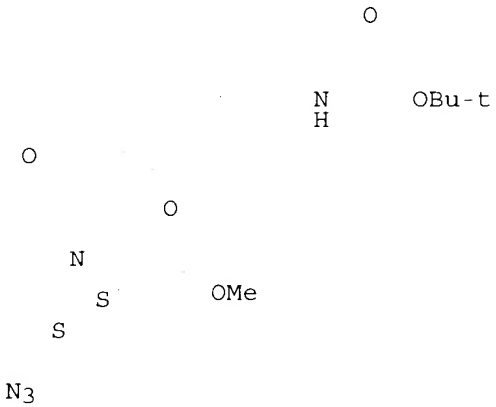
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C20 H28 N6 O4

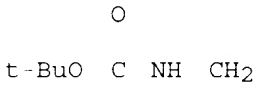
Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-1-[[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]cyclohexyl]carbonyl]-, methyl ester, (4S)- (9CI)
MF C19 H31 N5 O5

Absolute stereochemistry.

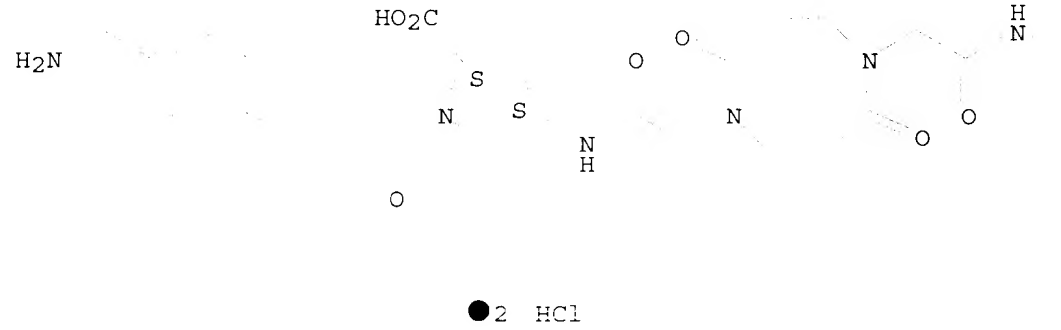


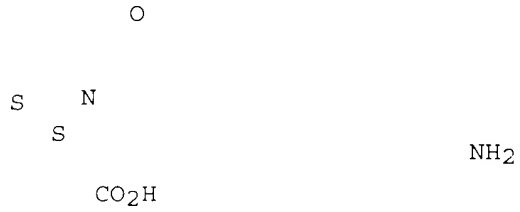


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C40 H52 N8 O10 . 2 Cl H

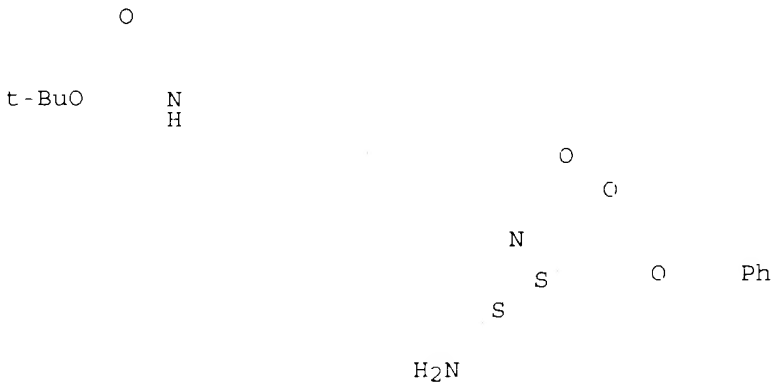
Absolute stereochemistry.





L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-amino-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, phenylmethyl ester, (4S)- (9CI)
MF C27 H35 N3 O5

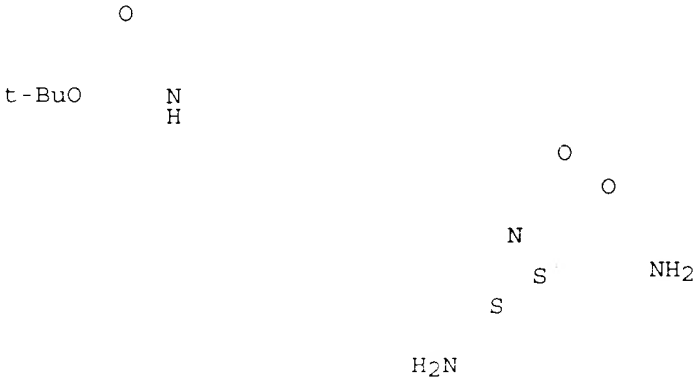
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C20 H30 N4 O4

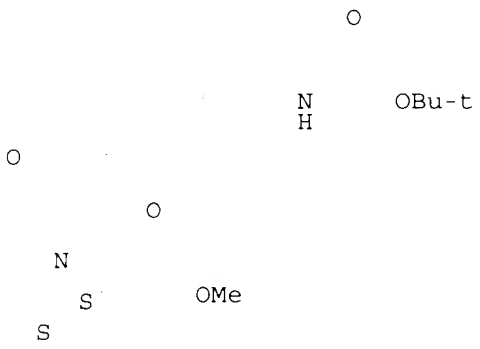
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

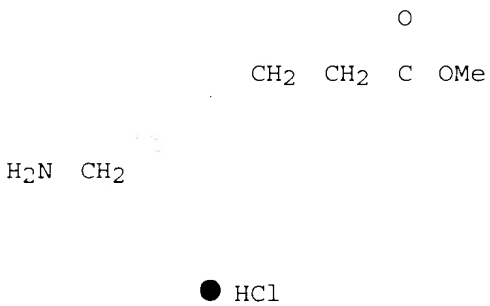
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-amino-1-[[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]cyclohexyl]carbonyl]-, methyl ester, (4S)- (9CI)
MF C19 H33 N3 O5

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

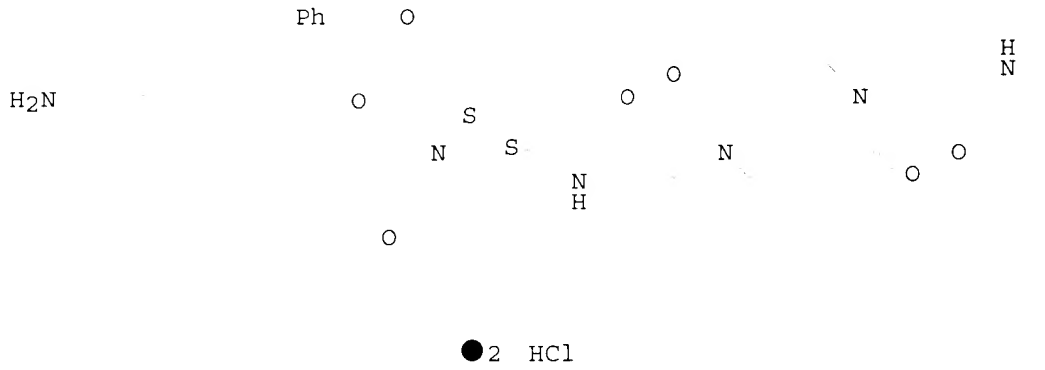
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzenepropanoic acid, 4-(aminomethyl)-, methyl ester, hydrochloride (9CI)
MF C11 H15 N O2 . Cl H



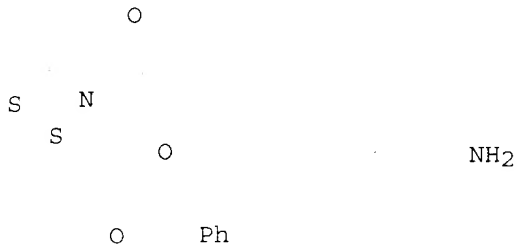
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C54 H64 N8 O10 . 2 Cl H

Absolute stereochemistry.

PAGE 1-A



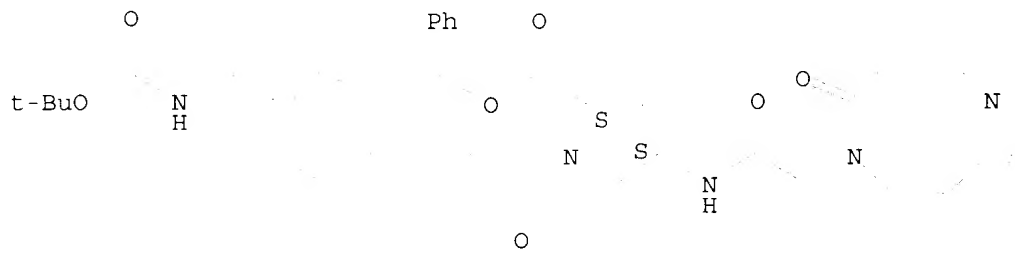
PAGE 1-B



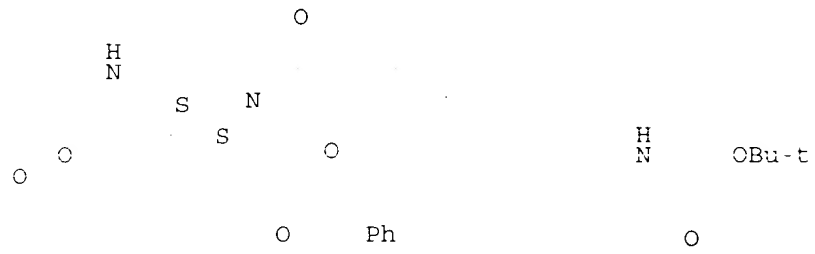
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C64 H80 N8 O14

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

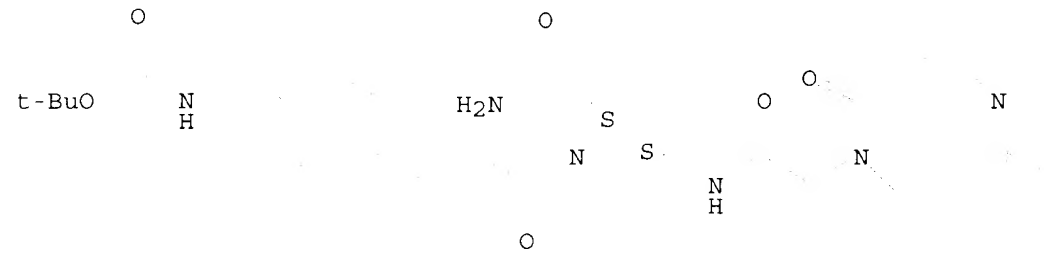


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

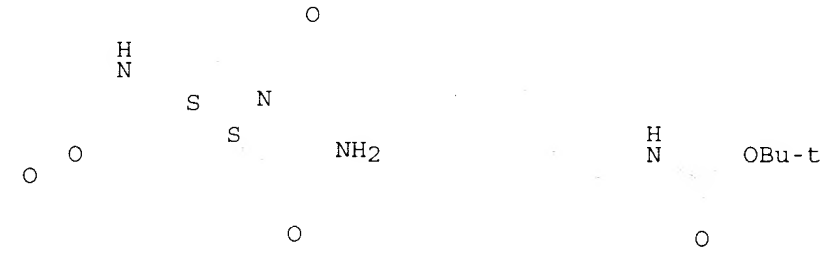
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C50 H70 N10 O12

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

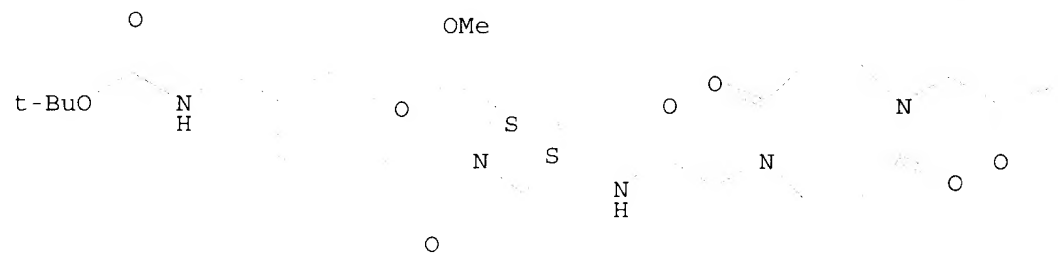


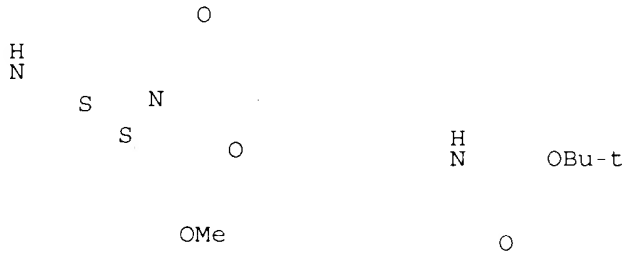
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C48 H76 N8 O14

Absolute stereochemistry.

PAGE 1-A





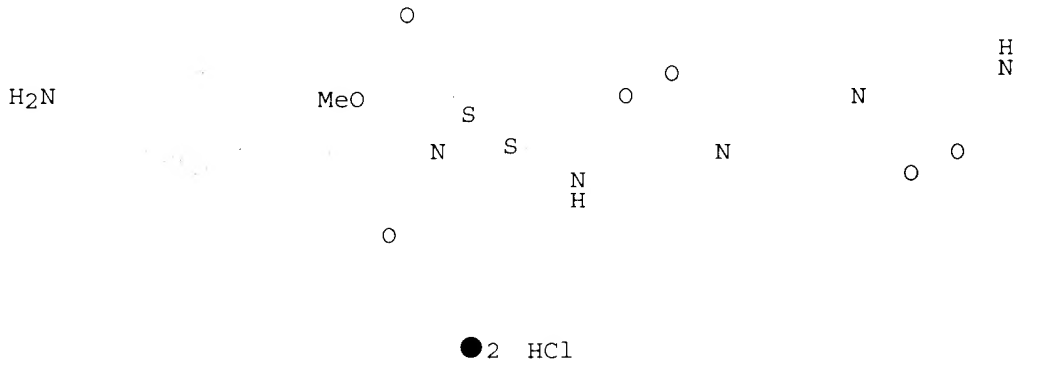
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Tryptase (9CI)
MF Unspecified
CI MAN

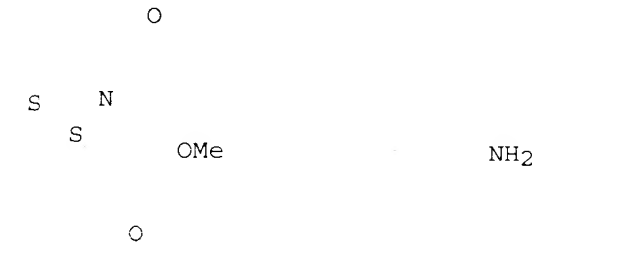
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C42 H56 N8 O10 . 2 Cl H

Absolute stereochemistry.



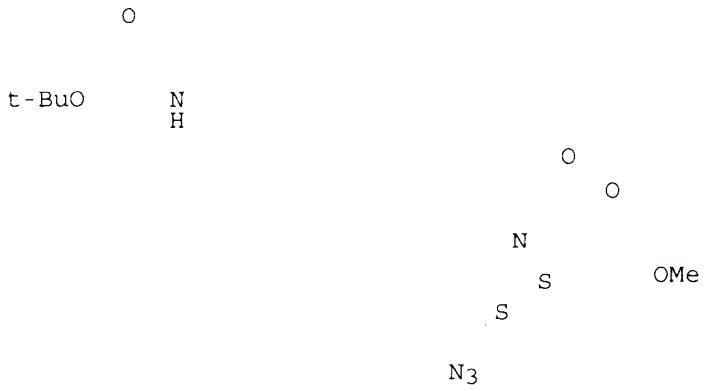
PAGE 1-B



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS

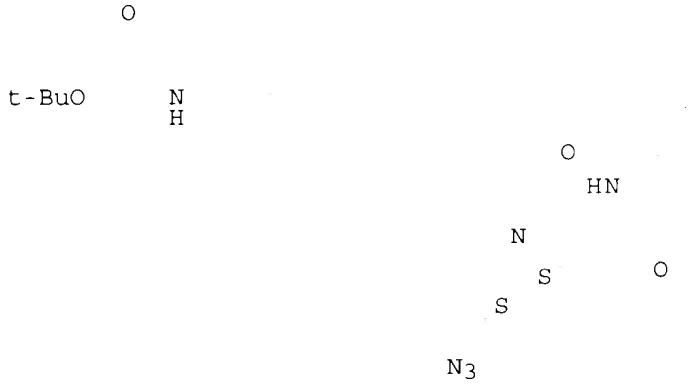
IN L-Proline, 4-azido-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, methyl ester, (4S)- (9CI)
MF C21 H29 N5 O5

Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Carbamic acid, [[4-[3-[(2S,4S)-4-azido-2-[(cyclopropylamino)carbonyl]-1-pyrrolidinyl]-3-oxopropyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI)
MF C23 H32 N6 O4

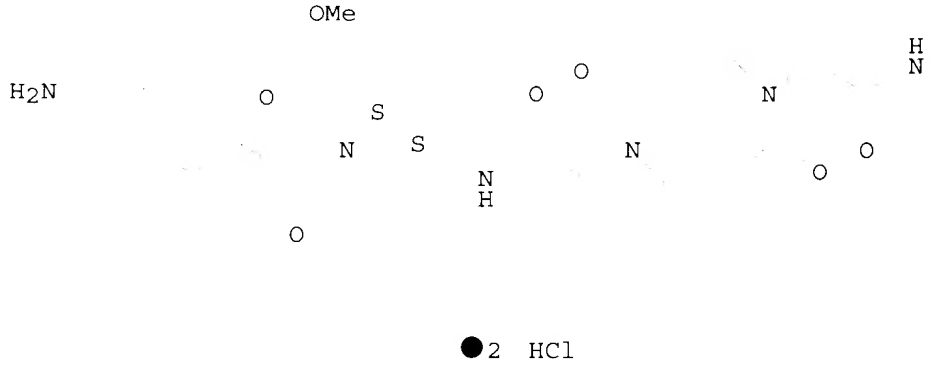
Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C38 H60 N8 O10 . 2 Cl H

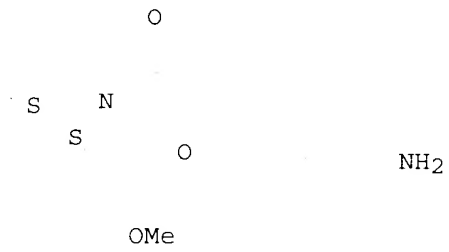
Absolute stereochemistry.

PAGE 1-A



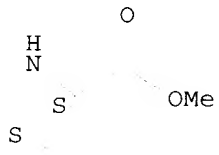
● 2 HCl

PAGE 1-B



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-, methyl ester, (4S)- (9CI)
MF C6 H10 N4 O2
CI COM

Absolute stereochemistry.



ALL ANSWERS HAVE BEEN SCANNED

DN 137:47190
TI Preparation of (fused) thiazolyl and thienyl-substituted N-(aminomethylbenzoyl)(hetero)arylglycinamides as tryptase inhibitors.
IN Lively, Sarah Elizabeth; Harrison, Martin James; Naylor, Neil Jason; Farthing, Christopher Neil; Waszkowycz, Bohdan
PA Tularik Limited, UK
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047762	A1	20020620	WO 2001-GB5526	20011212
WO 2001044226	A1	20010621	WO 2000-GB4764	20001213

PI WO 2002047762 A1 20020620 WO 2001-GB5526 20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2001044226 A1 20010621 WO 2000-GB4764 20001213
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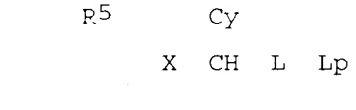
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2000-GB4764 W 20001213
GB 2001-14185 A 20010612
GB 1999-29552 A 19991214
WO 2000-GB2291 W 20000613

OS MARPAT 137:47190
GI



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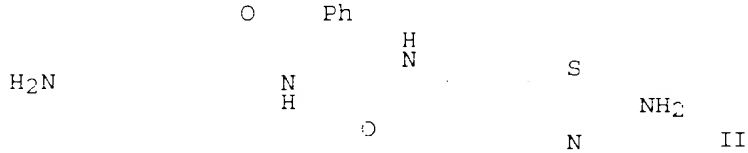


II

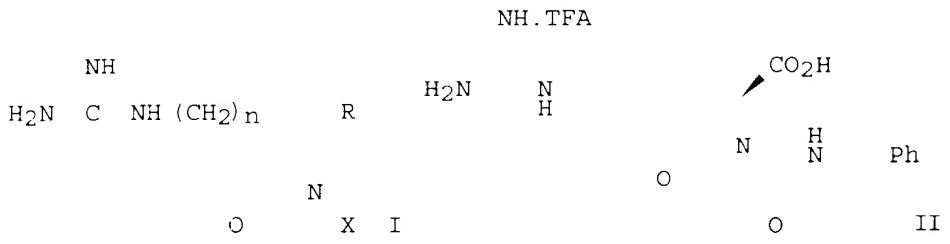
AB N-(3-aminomethylbenzoyl)aryl- and heteroarylglycinamides I [Cy = (un)substituted cycloalkyl, aryl, heterocyclyl, heteroaryl; L = CONR1(CH2)m; Lp = (un)substituted thiazolyl, thiazol-2-yl, 4-arylthiazol-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydrobenzothiazol-2-yl, etc.; m = 0, 1; R1 = H, alkyl, phenylalkyl; R5 = H, H2N, HO, H2NCH2, HOCH2; R6a = H, Me; X = CH:CH, CONR1, NHCO, NR1CH2, CH2O, CO2, CH2CH2] are prepd. as inhibitors of the serine protease tryptase for the treatment of asthma (no data). E.g., 2,6-diaminobenzothiazole (prepd. by redn. of 2-amino-6-nitrobenzothiazole) was coupled with N-Boc-D-phenylglycine, deprotected with F3CCO2H, the free .alpha.-amino group coupled with 3-(N-tert-butoxycarbonylaminomethyl)benzoic acid, and the product deprotected with F3CCO2H to give phenylglycinamide II. Formulations contg. I are given.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2002:389878 CAPLUS
TI Anti-inflammatory 1-aroyl-4-(m-aminomethylphenyl)piperidine derivatives
AU Anon.
SO Expert Opinion on Therapeutic Patents (2002), 12(5), 751-754
CODEN: EOTPEG; ISSN: 1354-3776
PB Ashley Publications Ltd.
DT Journal
LA English
AB A series of 1-aroyl-4-(m-aminomethylphenyl)**piperidine** derivs. and their 1-heteroaroyl analogs are claimed. These amines are low mol. wt. **inhibitors** of **tryptase**, some of which have reasonable potency. If combined with good pharmacokinetic properties this class of compds. may prove to be therapeutically useful in the treatment of asthma or allergic rhinitis.
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2002:6377 CAPLUS
DN 136:69695
TI Preparation of .beta.-lactam compounds as inhibitors of tryptase
IN Bisacchi, Gregory S.; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Schwinden, Mark D.; Xu, Zhongmin; Shi, Zhongping
PA Bristol-Myers Squibb Co., USA
SO U.S., 171 pp., Cont.-in-part of U. S. Ser. No. 336,253, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6335324	B1	20020101	US 1999-458847	19991213
PRAI	US 1998-90636P	P	19980625		
	US 1999-336253	B2	19990618		

OS MARPAT 136:69695
GI



AB Novel .beta.-lactam compds., e.g. of formula I [R = CO2H, alkoxycarbonyl, acyl, CO-heterocyclyl, etc.; X = acyl, CO-heterocyclyl, SO2-alkyl, aminoalkylphenyl, etc.; n = 1-6], are prepd. These compds. inhibit tryptase as well as other enzyme systems or are selective tryptase inhibitors and are useful as antiinflammatory agents particularly in the treatment of chronic asthma (no data). Thus, II was prepd. from (4S)-N-(tert-butyldimethylsilyl)azetidin-2-one-4-carboxylic acid, 1-chloro-3-iodopropane, N,N'-bis(benzyloxycarbonyl)-1-guanylpyrazole and benzyl isocyanate.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-**piperidinyl**-benzylamines for use as **tryptase inhibitors**
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2000-12362 A 20000522
US 2001-843126 A 20010426
OS MARPAT 136:5917
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 -

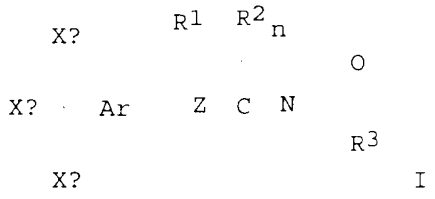
4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

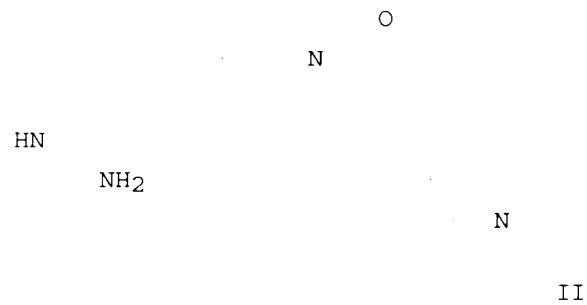
L2 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:798195 CAPLUS
DN 135:344381
TI Preparation of 1-aroyl-**piperidinyl** benzamidines as **inhibitors** of Factor Xa or **tryptase**
IN Pauls, Heinz; Gong, Yong; Levell, Julian; Astles, Peter C.; Eastwood, Paul R.
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001081310	A1	20011101	WO 2001-US13810	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002045613	A1	20020418	US 2001-841417	20010424
PRAI	US 2000-200066P	P	20000427		
	GB 2000-18306	A	20000726		

OS MARPAT 135:344381
GI



I



II

AB The title compds. [I; Z = C, N; ring C = 4-7 membered azaheterocyclyl, 4-7 membered azaheterocyclenyl; Ar = aryl, monocyclic heteroaryl, bicyclic azaheteroaryl; R1 = H, CH2OR12, CH2SR12, etc.; R2 = H, alkyl, aralkyl, etc.; R3 = cycloalkyl, cycloalkenyl, heterocyclyl, etc.; Xa, Xb, Xc = H, (hydroxy)NH, halo, etc.; R12 = H, alkyl, acyl, etc.], useful for the treatment of patients suffering from conditions which can be ameliorated by the administration of an inhibitor of Factor Xa or tryptase, were prepd. E.g., a multi-step synthesis of II.2F3CCO2H which showed Ki of 9.0 nM against Factor Xa, was given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:478090 CAPLUS
DN 135:298146
TI Dibasic inhibitors of human mast cell tryptase. Part 3: Identification of a series of potent and selective inhibitors containing the benzamidine functionality
AU Dener, J. M.; Rice, K. D.; Newcomb, W. S.; Wang, V. R.; Young, W. B.; Gangloff, A. R.; Kuo, E. Y.-L.; Cregar, L.; Putnam, D.; Wong, M.
CS Departments of Medicinal Chemistry, Biochemistry, and Enzymology, Axys Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(13), 1629-1633
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB A survey of charged groups and linkers for a series of sym. and unsym. dibasic inhibitors is described, leading to several classes of potent and selective inhibitors. The inhibitors synthesized and tested were related to the known inhibitor APC-1390. In particular, the benzamidine functionality was identified as the most potent charged group investigated.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:472693 CAPLUS
DN 135:76895

TI Preparation of tryptase inhibiting alkynediol piperazinecarboxylate esters

IN Baer, Thomas; Stadlwieser, Josef; Ulrich, Wolf-Ruediger; Dominik, Andreas; Bundschuh, Daniela; Zech, Karl; Sommerhoff, Christian; Martin, Thomas

PA Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany

SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

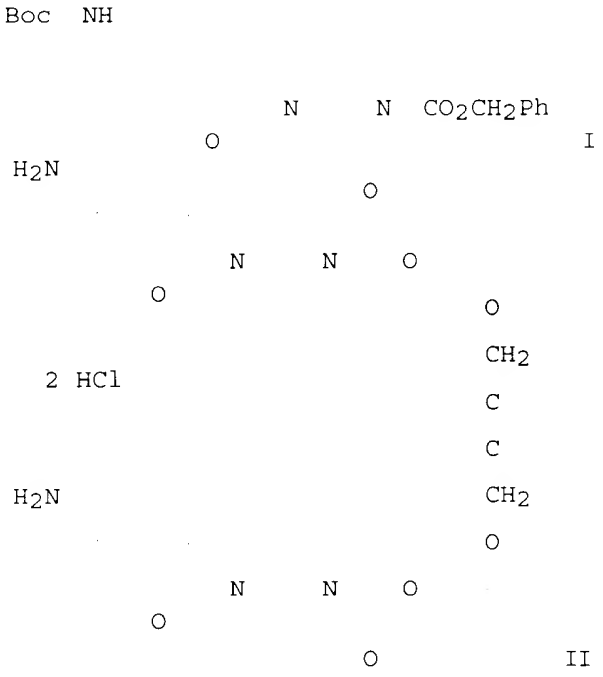
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046168	A1	20010628	WO 2000-EP12838	20001216

PI W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI EP 1999-125384 A 19991220

OS MARPAT 135:76895

GI



AB Alkynes K2-A2-U2(C.tplbond.C)nU1-A1-K1 [n = 1, 2; U1, U2 = CH2, CH2CH2, CH2CH2CH2, CH2CH2CH2CH2, Me2C; A1 = A3-B1-A5; A2 = A4-B2-A6; A3, A4 = CO, CO2, CONH, NHCO, OCONH, NHCO2, NHCONH, OCO2, O(CH2)pCO, O(CH2)mOCO, O(CH2)mNHCO; p, m = 1, 2, 3, 4; A5, A6 = CO, CONH, NHCO, OCONH, NHCO2, NHCONH, OCO2; B1, B2 = alkylene, cyclohexylene, phenylene, piperazinylene, **piperidinylene**; K1 = B3-X1, B3-Y1, B3-Z1-B5-X1; K2 = B4-X2, B4-Y2, B4-Z2-B6-X2; B3, B4 = bond, alkylene; B5, B6 = bond alkylene; X1, X2 = H2N, H2NCO, amidino; Y1, Y2 = imidazolyl; Z1, Z2 = pyridinylene, 6-methyl-5,2-pyridinylene, **piperidinylene**, 3,6-indazolylene, 3,6-indolylene, phenylene, cyclohexylene] and their salts and N-oxides were prepd., possessed **tryptase inhibiting** activities, and were medicaments for the treatment of airway (pulmonary) disorders.

Thus, condensation of trans-4-[(tert-butoxycarbonylamino)methyl]cyclohexan ecarboxylic acid and 1-(benzyloxycarbonyl)piperazine in CH2Cl2 contg. 1-hydroxybenzotriazole gave the (cyclohexylcarbonyl)piperazinecarboxylate I. Debenzylation of I and subsequent esterification with 1,4-bis(2-hydroxyethoxy)-2-butyne and deblocking gave the bis(cyclohexylcarbonylpiperazinecarboxylate) ester salt II which possessed an apparent dissocn. const. of 0.086 .mu.M for its **tryptase-inhibitor** complex.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:454760 CAPLUS
DN 135:165939
TI Tryptase-induced airway microvascular leakage in guinea pigs: involvement of tachykinins and leukotrienes
AU Greenfeder, Scott; Sehring, Susan; McHugh, Nansie; Corboz, Michel; Rivelli, Maria; Anthes, John C.; Billah, Motasim; Egan, Robert W.; Chapman, Richard W.
CS Department of Allergy, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SO European Journal of Pharmacology (2001), 419(2/3), 261-267
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB **Tryptase**, a serine protease synthesized by and stored in mast cells, is implicated as an important mediator in the pathogenesis of airway inflammation. In this study, **tryptase** was evaluated for its ability to induce microvascular leakage into the airways of guinea pigs. Dose- and time-dependent increases in airway microvascular leakage were produced by intratracheal **tryptase** (0.3-3 .mu.g). Intratracheal **tryptase** (3-30 .mu.g) had no effect on airway tone as measured by pulmonary insufflation pressure. **Tryptase**-induced airway microvascular leakage was partially blocked by the tachykinin NK1 receptor antagonist CP 99994 [(+)-(2S,3S)-3-(2-methoxybenzylamino)-2-phenylpiperidine] and an **inhibitor** of leukotriene formation SCH 37224 (1-(1,2-dihydro-4-hydroxy-2-oxo-1-phenyl-1,8-naphthyridin-2-yl)**pyrrolidinium**, hydroxide inner salt). Neither CP 99994 nor SCH 37224 **inhibited tryptase** proteolytic activity in-vitro. Pretreatment of guinea pigs with histamine H1 receptor antagonists or a tachykinin NK2 receptor antagonist had no affect on the airway microvascular leakage induced by **tryptase**. It is speculated that **tryptase** may be important in the pathogenesis of airway inflammation, particularly in disorders that involve increased airway microvascular leakage such as asthma.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2000:535126 CAPLUS
DN 133:150919
TI Preparation of peptidyl heterocyclic ketones useful as tryptase inhibitors
IN Costanzo, Michael J.; Maryanoff, Bruce E.; Yabut, Stephen C.
PA Ortho-McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000044733	A1	20000803	WO 2000-US883	20000113

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1147097 A1 20011024 EP 2000-909902 20000113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000007778 A 20020604 BR 2000-7778 20000113

NO 2001003666 A 20010926 NO 2001-3666 20010726

PRAI US 1999-117602P P 19990127

WO 2000-US883 W 20000113

OS MARPAT 133:150919

AB Peptidyl heterocyclic ketones A-NRCR1R2CO-E [A = substituted cycloalkylcarbonyl, norbornanecarbonyl, norbornenecarbonyl, adamantanecarbonyl, arylcarbonyl, heteroarylcarbonyl, aminoalkylcarbonyl, an amino acid or dipeptide residue, etc.; R, R1 = H, alkyl; R2 = amino-, guanidino-, alkylguanidino-, dialkylguanidino-, amidino-, alkylamidino-, dialkylamidino-, or alkoxyalkyl, (un)substituted Ph, benzyl, pyridyl, pyridyl-, pyrimidyl-, triazinyl-, or imidazoalkyl, imidazolinyl-, N-amidinopiperazinyl-, hydroxy-, alkylamino-, dialkylamino-, N-amidinopiperidinyl-, or 4-aminocyclohexylalkyl; E = (un)substituted heterocyclyl] and their pharmaceutically acceptable salts and prodrugs were prepd. as **tryptase inhibitors** and are therefore effective for the prevention and treatment of inflammatory diseases assocd. with the respiratory tract, such as asthma and allergic rhinitis. Thus, (2S,4R)-1-acetyl-N-[(1S)-4-[(aminoiminomethyl)amino]-1-(2-benzothiazolylcarbonyl)butyl]-4-hydroxy-2-**pyrrolidinecarboxamide** was prepd. by a seven-step procedure starting from Boc-Arg(Ts)-OH (Boc, tert-butoxycarbonyl, Ts = tosyl), benzothiazole, and trans-1-acetyl-4-benzyloxyl-L-proline and showed IC50 = 0.036 .+-. 0.031 .mu.M for **inhibition** of **tryptase**.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS

AN 2000:445771 CAPLUS

DN 133:248787

TI Selective inhibition of trypsin by (2R,4R)-4-phenyl-1-[N.alpha.-(7-methoxy-2-naphthalenesulfonyl)-L-arginyl]-2-piperidinecarboxylic acid

AU Hijikata-Okunomiya, Akiko; Tamao, Yoshikuni; Kikumoto, Ryoji; Okamoto, Shosuke

CS Faculty of Health Science, Kobe University School of Medicine, Kobe, 654-0142, Japan

SO Journal of Biological Chemistry (2000), 275(25), 18995-18999
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB Evidence is accumulating indicating that trypsin stimulates divergent cellular reactions through the proteinase-activated receptor, in addn. to its role as the digestive enzyme. In this report, we introduce (2R,4R)-4-phenyl-1-[N.alpha.-(7-methoxy-2-naphthalenesulfonyl)-L-arginyl]-2-**piperidinecarboxylic** acid as a potent and selective trypsin **inhibitor**. The agent **inhibited** trypsin competitively with the Ki value of 0.1 .mu.M. It **inhibited** thrombin weakly (Ki = 2 .mu.M) and did not **inhibit** plasmin, plasma kallikrein, urokinase, and mast cell **tryptase** (Ki values for these enzymes are >60 .mu.M). Comparative studies with several established proteinase

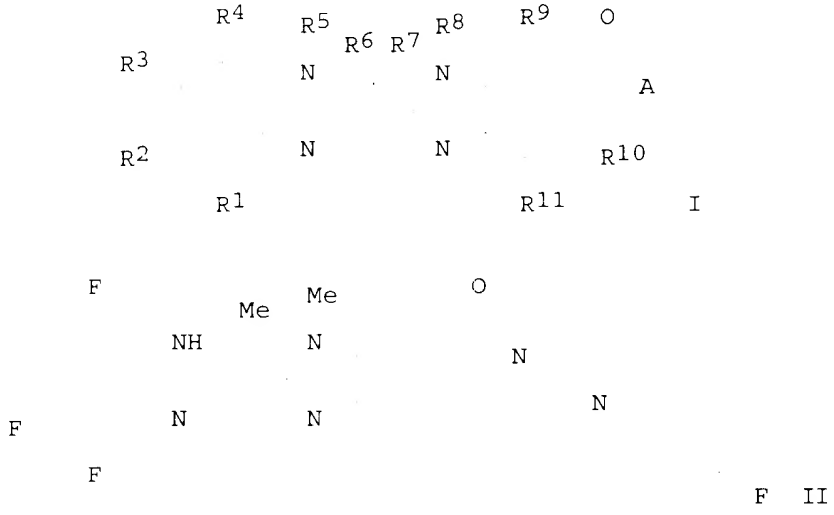
inhibitors revealed that the compd. was the first small mol. wt. trypsin **inhibitor** without **tryptase inhibitory** activity. A docking study has provided a plausible explanation for the mol. mechanism of the selective **inhibition** showing that the agent fits into the active site of trypsin without any severe collision but that it comes into clash at the 4-Ph group of **piperidine** ring against the "60-insertion loop" of thrombin and at the 7-methoxy-2-naphthalenesulfonyl group against Gln98 of **tryptase**.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2000:241202 CAPLUS
DN 132:265195
TI Preparation of bis-benzimidazoles as tryptase inhibitors
IN Mittendorf, Joachim; Henning, Rolf; Raddatz, Siegfried; Schlemmer, Karl-heinz; Hiraoka, Makiko; Kadono, Hiroshi; Mogi, Muneto; Moriwaki, Toshiya; Murata, Toshiki; Sakakibara, Sachiko; Shimada, Mitsuyuki; Yoshida, Nagahiro; Yoshino, Takashi
PA Bayer Yakuhin, Ltd., Japan; et al.
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020401	A1	20000413	WO 1999-JP5319	19990929
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9959981	A1	20000426	AU 1999-59981	19990929
	EP 1117651	A1	20010725	EP 1999-969935	19990929
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002526537	T2	20020820	JP 2000-574518	19990929

PRAI US 1998-102711P P 19981001
US 1999-117269P P 19990126
US 1999-123277P P 19990309
WO 1999-JP5319 W 19990929
OS MARPAT 132:265195
GI



F II

AB Title compds. (I) [wherein R1, R2, R3, and R4 = independently H, OH, or halogen; R5 and R8 = independently H or alkyl; R6 and R7 = independently H, OH, halogen, alkyl, or alkoxy; R9, R10, and R11 = independently H, halogen, NO2, CN, or CF3; A = non-arom. 5-7-membered N-heterocycle, etc.] were prepd. for use in the treatment of diseases assocd. with tryptase activity including allergic, inflammatory, and related immunol. diseases, in particular asthma, allergic rhinitis, allergic conjunctivitis, and allergic dermatitis. Examples include syntheses for 70 compds. and their intermediates, tryptase inhibitory activity data, and bioavailability data. For instance, refluxing Et 2-(4,6,7-trifluoro-1H-benzimidazol-2-yl)propionate (prepn. given) with 4-amino-3-(methylamino)benzoic acid in DMPU produced the bis-benzimidazole (66%). Subsequent reaction with 1-(4-fluorophenyl)piperazine in the presence of N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide.HCl, 1-hydroxybenzotriazole, and TEA in DMF yielded II (73%). II gave a Ki of 3.0 nM in the presence of ZnCl2 in a human tryptase inhibition assay. Compared to a known tryptase inhibitor, II showed improved oral bioavailability in rats, dogs, and primates in pharmacokinetics tests (72% vs. 0.3%, 74% vs. 0.2-7%, and 100% vs. not detd., resp.).

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1999:819347 CAPLUS
DN 132:64103
TI Preparation of amidino and guanidino azetidinone compounds as tryptase inhibitors
IN Bisacchi, Gregory; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Xu, Zhongmin; Shi, Zhongping; Schwinden, Mark D.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 326 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9967215	A1	19991229	WO 1999-US13811	19990618

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,

MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9946950	A1	20000110	AU 1999-46950	19990618
EP 1089973	A1	20010411	EP 1999-930402	19990618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9911373	A	20010918	BR 1999-11373	19990618
JP 2002518478	T2	20020625	JP 2000-555869	19990618
NO 2000006380	A	20001214	NO 2000-6380	20001214
PRAI US 1998-90636P	P	19980625		
WO 1999-US13811	W	19990618		

OS MARPAT 132:64103
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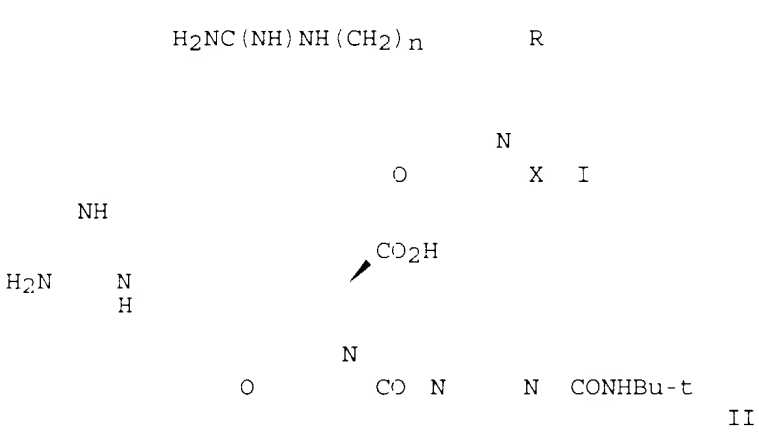


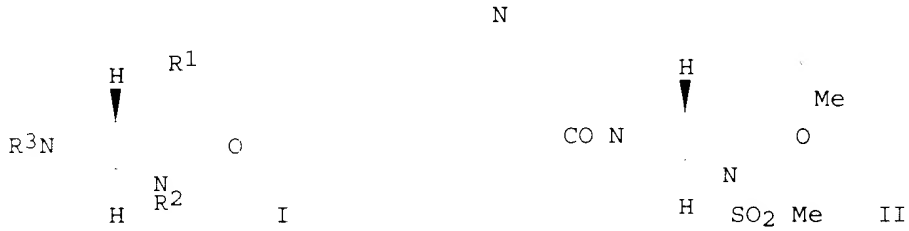
AB Novel .beta.-lactam compds., e.g. of formula I [R - CO2H, CONH-alkyl, etc.; X = CONH(CH2)2NHCO2alkyl, etc.; n = 1-6;], are prepd. as inhibitors of in vivo enzyme systems including tryptase, thrombin, trypsin, factor Xa, factor VIIa, and urokinase-type plasminogen activator (no data). The tryptase activity makes the title compds. useful as antiinflammatory agents in the treatment of chronic asthma and allergic rhinitis. Thus, II was prepd. from (4S)-N-(tert-butyldimethylsilyl)azetidin-2-one-4-carboxylic acid, tert-butyl-1-piperazine carboxylate and tert-Bu isocyanate.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1999:194149 CAPLUS
DN 130:223259
TI Preparation of pyrrolopyrrolidine derivatives and their use as serine protease inhibitors
IN Coote, Steven John; Dowle, Michael Dennis; Finch, Harry; Hann, Michael Menteith; Kelly, Henry Anderson; MacDonald, Simon John Fawcett; Pegg, Neil Anthony; Ramsden, Nigel Grahame; Watson, Nigel Stephen
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 9912935	A1	19990318	WO 1998-EP5744	19980907
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9896243	A1	19990329	AU 1998-96243	19980907
	EP 1015456	A1	20000705	EP 1998-950011	19980907
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515906	T2	20010925	JP 2000-510742	19980907
PRAI	GB 1997-19161	A	19970909		
	WO 1998-EP5744	W	19980907		
OS	MARPAT 130:223259				
GI					

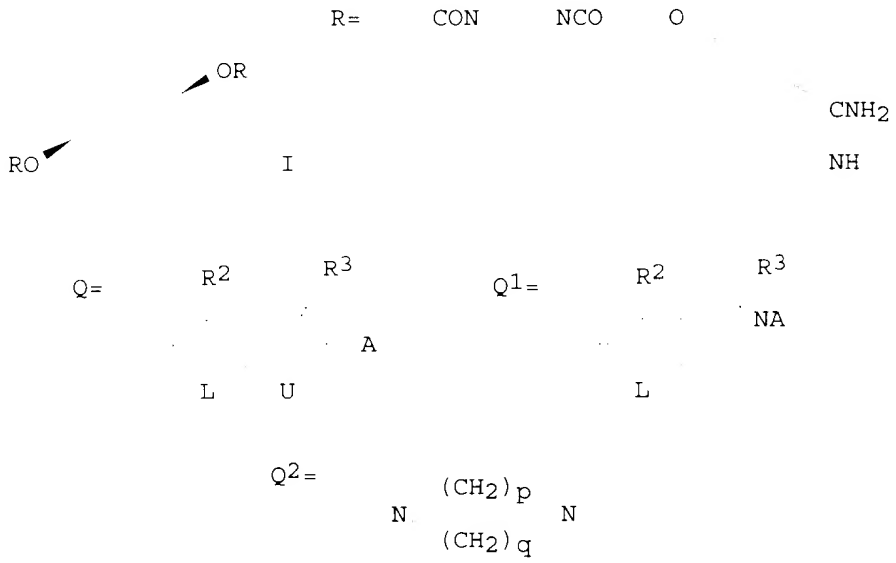


AB Trans-hexahydropyrrolo[3,4-b]pyrrol-2-ones I [R1 = moiety adapted to fit the S1 specificity subsite of the enzyme; R2 = moiety adapted to optimize potency, pharmacokinetics, pharmacodynamics, selectivity, and enzyme kinetics; R 3 = moiety adapted to optimize potency, pharmacokinetics, pharmacodynamics, and physicochem. properties] were prepd. as antiviral serine protease **inhibitors**. Thus, the hydrochloride salt of trans-hexahydropyrrolo[3,4-b]pyrrol-2-one II was prepd. starting from trans-4-nitro-1-(phenylmethyl)-3-**pyrrolidineacetic** acid Et ester, allyl iodide, and 4-(**piperidin**-1-yl)-but-2-enoic acid hydrochloride. The prepd. compds. were tested for **inhibition** of viral serine protease, human mast cell **tryptase**, trypsin, tissue plasminogen activator, Factors VIIa, Xa, XIa, XIIa, plasmin, chymotrypsin, and cathepsin G.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1999:194135 CAPLUS
DN 130:237590
TI Preparation of bis(piperazin-1-ylcarbonylmethoxy)cyclooctane and -benzene and related derivatives as selective tryptase inhibitors
IN Ono, Shinichiro; Takeuchi, Masahiro; Sakashita, Hiroshi; Kuwahara, Shigeki; Naito, Koji; Naito, Youichiro; Imagawa, Takashi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9912918	A1	19990318	WO 1998-JP3978	19980904
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9889974	A1	19990329	AU 1998-89974	19980904
PRAI	JP 1997-241387		19970905		
	WO 1998-JP3978		19980904		
OS	MARPAT 130:237590				
GI					



AB Claimed are compds. represented by general formula of ZCOYCO(CH2)nXWX1(CH2)n1COY1COZ1 [Z, Z1 = Q, Q1; wherein A = E1E11NC(:NE2), E1E11NC(:NE2)NE3, E1E11N(CH2)d, E1E11NCO; E1, E11, E2, E3 = H, aralkyl, alkyl, amidino, guanidino, protecting group for primary amino group; E2 is addnl. OH; or E1E11N = heterocyclyl contg. addnl. heteroatoms; d = 1-3; Z, Z1 = E1E11C(:NE2), E1E2N (CH2)d (d = 1,3); L = O, NR4, S, SO2, CH2; R4 = H, alkyl, cycloalkyl, aralkyl, acyl; U = :CH, :N; R2, R3 = H, alkyl, halo, CF3, OH, NH2, acyl, alkoxy; W = (CH2)l (l = 1-10), (un)substituted C3-14 cycloalkylene; Y, Y1 = Q2 (p, q = 1-3), NH(CH2)cNH (c = 1-8); n, n1 = 0,1] or pharmacol. acceptable salts thereof, a pharmaceutical compn. thereof, and use thereof as a pharmaceutical, in particular a tryptase inhibitor and allergy inhibitor based on tryptase inhibition activity. The compds. and pharmacol. acceptable salts thereof have an excellent tryptase inhibitory activity with high selectivity, are orally administrable, and have a reduced toxicity, thus being useful for pharmaceuticals, for example, those for prophylaxis or therapy of allergic diseases such as allergic rhinitis, hypersensitive pneumonia, pulmonary fibrosis, and bronchial asthma. Thus, cis-1,5-bis(piperazin-1-ylcarbonyloxy)cyclooctane dihydrochloride was condensed with 5-[1-(benzyloxycarbonylamino)-1-iminomethyl]benzofuran-2-ylcarboxylic acid using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOBt, and Et3N in DMF for 17 h, followed by hydrogenolysis over 10% Pd-C in CHCl3/MeOH to give the

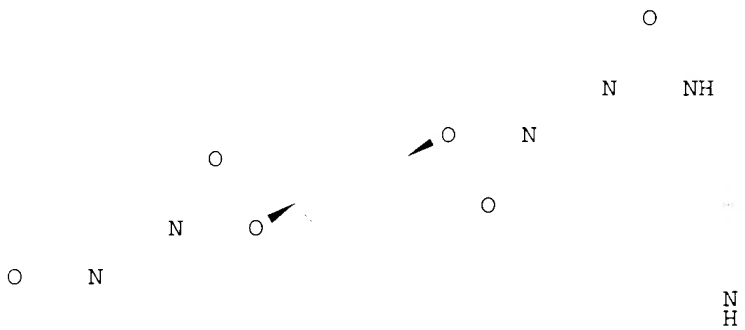
title compd. (I).2HCl. I.2HCl inhibited human tryptase and human thrombin with Ki of 2.5 .times. 10-12 and 4.5 .times. 10-5 M, resp.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1998:102855 CAPLUS
DN 128:167443
TI Novel compounds [cyclooctylene bis(piperazinecarboxylates) and analogs] and compositions for treating diseases associated with tryptase activity
IN Dener, Jeffrey Mark; Kuo, Elaine Yee-Lin; Rice, Ken Duane; Wang, Vivian Rueywen; Young, Wendy Beth
PA Arris Pharmaceutical Corporation, USA; Dener, Jeffrey Mark; Kuo, Elaine Yee-Lin; Rice, Ken Duane; Wang, Vivian Rueywen; Young, Wendy Beth
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804537	A1	19980205	WO 1997-US13422	19970730
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739670	A1	19980220	AU 1997-39670	19970730
	AU 733621	B2	20010517		
	EP 934293	A1	19990811	EP 1997-937066	19970730
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1226892	A	19990825	CN 1997-196877	19970730
	CN 1073103	B	20011017		
	JP 2001509787	T2	20010724	JP 1998-509136	19970730
	FI 9900171	A	19990323	FI 1999-171	19990129
	NO 9900433	A	19990325	NO 1999-433	19990129
	KR 2000029679	A	20000525	KR 1999-7000757	19990129
	LV 12291	B	20000420	LV 1999-27	19990218
	LT 4587	B	19991227	LT 1999-19	19990301
	LV 12458	B	20000920	LV 2000-30	20000225
	LV 12459	B	20000920	LV 2000-31	20000225
PRAI	US 1996-23139P	P	19960730		
	US 1997-895772	A	19970717		
	US 1996-23139	A	19960730		
	WO 1997-US13422	W	19970730		
	LV 1999-990027	A3	19990218		

OS MARPAT 128:167443
GI



II

AB The invention relates to novel compds. (R1X1X2X3X4)-X5-(X6X7X8X9R2) (I), which are **tryptase inhibitors**, and their pharmaceutically acceptable salts and N-oxides, as well as their uses as therapeutic agents, and methods of their prepn. [wherein X5 = (hetero)cycloalkylene, (hetero)arylene; X4, X6 = bond, alkylene; X1, X9 = bond, CO, CO2, OCO, CONR3, NR3CO, etc.; R3 = H, alkyl, cycloalkyl; X3, X7 = CO, CO2, OCO, CONR3, NR3CO, etc.; X2, X8 = (hetero)alkylene and/or cycloalkylene; R1 = amino, amidino, guanidino, certain N-heterocycles, etc., with optional (hetero)alkylene or other bridge; R2 = amino, 1-iminoethyl, methylamino, or certain N-heterocycles, with required or optional alkylene or other bridge]. The compds. are useful for treating a variety of conditions, including asthma, rheumatoid arthritis, and conjunctivitis. For instance, tert-Bu 4-[(4-guanidinobenzyl)carbamoyl]-1-piperazinecarboxylate trifluoroacetate underwent deprotection with CF3CO2H and amidation with cis-1,5-cyclooctylene chloroformate 4-(tert-butoxycarbonyl)-1-piperazinecarboxylate (77%), followed by a second deprotection and reaction with tert-Bu 4-(2-isocyanatoethyl)-1-**piperidinecarboxylate**, to give title compd. II. Compds. I **inhibited** human **tryptase** in vitro with IC50 in the range of 0.0001 to 41 .mu.M.

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5 CH      C
          4
            Cy   CH2 NH2
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE


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=> d l11
L11 HAS NO ANSWERS
L11             SCR 1841 OR 1840


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INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

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                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       337291 TO   352989
PROJECTED ANSWERS:               0 TO        0

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=> s l7 and l11 not l9 ful
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SEARCH TIME: 00.00.21
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FILE 'CAPLUS' ENTERED AT 15:38:26 ON 03 SEP 2002
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FILE COVERS 1907 - 3 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 2 Sep 2002 (20020902/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l15
L16 2 L15

=> d bib abs 1-2

L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2000-12362 A 20000522
US 2001-843126 A 20010426

OS MARPAT 136:5917

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1995:546553 CAPLUS
DN 122:290875
TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 32 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4234295	A1	19940414	DE 1992-4234295	19921012
	EP 592949	A2	19940420	EP 1993-116244	19931007
	EP 592949	A3	19940810		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2108093	AA	19940413	CA 1993-2108093	19931008
	JP 06199788	A2	19940719	JP 1993-252019	19931008
	FI 9304460	A	19940413	FI 1993-4460	19931011
	NO 9303647	A	19940413	NO 1993-3647	19931011
	NO 180232	B	19961202		
	NO 180232	C	19970312		
	AU 9348939	A1	19940428	AU 1993-48939	19931011
	AU 668765	B2	19960516		
	ZA 9307502	A	19950411	ZA 1993-7502	19931011
	CN 1087904	A	19940615	CN 1993-118925	19931012
	US 5442064	A	19950815	US 1993-135041	19931012
PRAI	DE 1992-4234295		19921012		

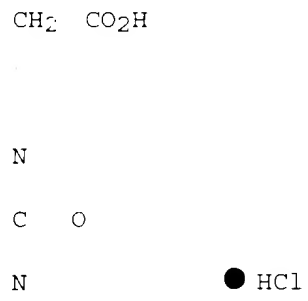
OS MARPAT 122:290875

AB ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene,

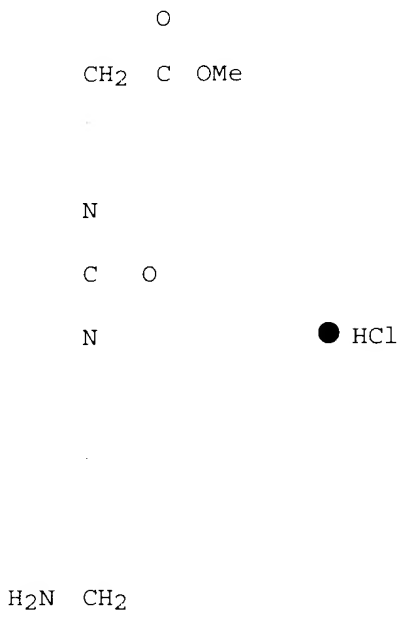
etc.; D = CH2, CH2CH2, CO, CH2CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO2R5; R5 = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O2N)C6H4O2CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC50 of 4.300nM against platelet aggregation in vitro.

=> d hitstr 2

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
IT **162996-75-0P 162996-88-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as platelet aggregation inhibitors)
RN 162996-75-0 CAPLUS
CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 162996-88-5 CAPLUS
CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)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C O
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HCl
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7 C       G1 10

8 C       C 11


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REP G1=(1-2) CH
VPA 15-3/4/5 U
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   4  11
NUMBER OF NODES IS  16

STEREO ATTRIBUTES: NONE


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SEARCH TIME: 00.00.03

L3          465 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               141.80     142.01

FILE 'CAPLUS' ENTERED AT 13:42:21 ON 03 SEP 2002
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FILE COVERS 1907 - 3 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 2 Sep 2002 (20020902/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l3
L4 2 L3

=> d bib abs 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	GB 2000-12362	A	20000522
	US 2001-843126	A	20010426

OS MARPAT 136:5917
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was

coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1995:546553 CAPLUS
DN 122:290875
TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 32 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 4234295	A1	19940414	DE 1992-4234295	19921012
EP 592949	A2	19940420	EP 1993-116244	19931007
EP 592949	A3	19940810		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2108093	AA	19940413	CA 1993-2108093	19931008
JP 06199788	A2	19940719	JP 1993-252019	19931008
FI 9304460	A	19940413	FI 1993-4460	19931011
NO 9303647	A	19940413	NO 1993-3647	19931011
NO 180232	B	19961202		
NO 180232	C	19970312		
AU 9348939	A1	19940428	AU 1993-48939	19931011
AU 668765	B2	19960516		
ZA 9307502	A	19950411	ZA 1993-7502	19931011
CN 1087904	A	19940615	CN 1993-118925	19931012
US 5442064	A	19950815	US 1993-135041	19931012
PRAI DE 1992-4234295		19921012		

OS MARPAT 122:290875
AB ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene, etc.; D = CH2, CH2CH2, CO, CH2CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO2R5; R5 = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O2N)C6H4O2CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC50 of 4.300nM against platelet aggregation in vitro.

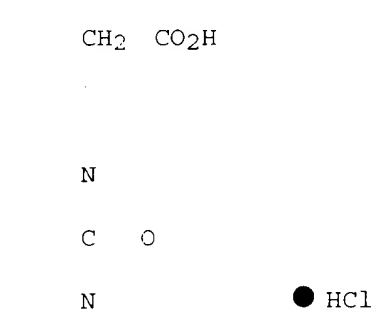
=> d hitstr 2

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
IT **162996-75-0P 162996-88-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as

platelet aggregation inhibitors)

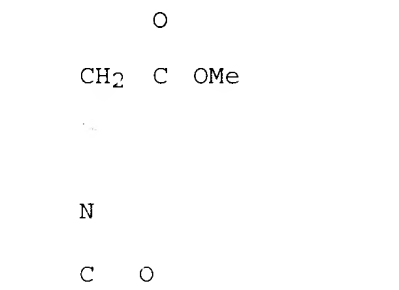
RN 162996-75-0 CAPLUS

CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 162996-88-5 CAPLUS

CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



AN 2002:675993 CAPLUS
DN 137:216874
TI Acylated piperidine derivatives, specifically 1-(pyrrolidinylcarbonyl)piperidines, 1-(piperidinylcarbonyl)piperidines, and analogs, as melanocortin-4 receptor agonists, and their pharmaceutical compositions and therapeutic uses
IN Ujjainwalla, Feroze; Chu, Lin; Goulet, Mark T.; Lee, Bonnie; Warner, Daniel; Wyvratt, Matthew J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002068388	A2	20020906	WO 2002-US5724	20020225
	WO 2002068388	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-272258P P 20010228
US 2001-300118P P 20010622
OS MARPAT 137:216874
GI

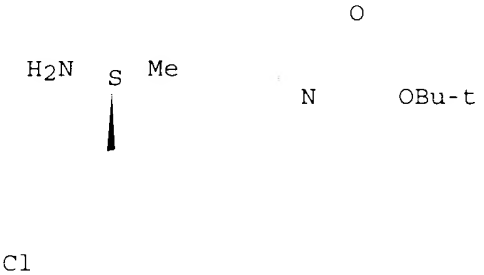
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Certain novel 4-substituted N-acylated piperidine derivs., specifically I, are agonists of the human melanocortin receptor(s) and, in particular, are selective agonists of the human melanocortin-4 receptor (MC-4R) [wherein: p = 1 or 2; q = 0, 1, or 2; n = 0, 1, or 2; R1 = H, amidino, alkyliminoyl, (un)substituted alkyl, (CH2)n-G1 [G1 = (un)substituted cycloalkyl, Ph, naphthyl, or heteroaryl]; R2 = (un)substituted Ph, naphthyl, or heteroaryl; X = alkyl, (CH2)n-G2 [G2 = (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl, heterocyclyl, cyano, CONH2, CO2H, OH, NH2, and various derivs.] where any of (CH2)n may also be substituted; including pharmaceutically acceptable salts]. They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. Approx. 180 invention compds. I and approx. 25 intermediates were prepd. For instance, (2-bromo-5-chlorophenyl)acetic acid underwent a sequence of Me esterification, coupling with tert-Bu 4-[[(trifluoromethyl)sulfonyl]oxy]-3,6-dihydropyridine-1(2H)-carboxylate via a boronate ester, removal of the BOC group, and amidation with (3S,4R)-1-(tert-butyl)-4-(2,4-difluorophenyl)pyrrolidine-3-carboxylic acid. The unsatd. amide-ester underwent hydrogenation, sapon. of the ester, and amidation with MeNH2.HCl, to give title compd. II. Representative compds. I bound to cloned human MC-4R in vitro with IC50 values generally below 2 .mu.M, and also acted as agonists toward cloned human MCR in a functional assay with EC50 values less than 1 .mu.M.
IT **455957-91-2P**, tert-Butyl 4-[2-((1S)-1-aminoethyl)-4-

chlorophenyl]piperidine-1-carboxylate **455957-92-3P**, tert-Butyl 4-[2-[(1S)-1-(acetylamino)ethyl]-4-chlorophenyl]piperidine-1-carboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of acylated piperidine derivs., particularly (pyrrolidinylcarbonyl)piperidines, (piperidinylcarbonyl)piperidines, and analogs, as melanocortin-4 receptor agonists)

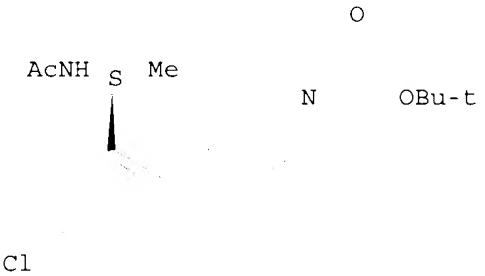
RN 455957-91-2 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[2-[(1S)-1-aminoethyl]-4-chlorophenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 455957-92-3 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[2-[(1S)-1-(acetylamino)ethyl]-4-chlorophenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

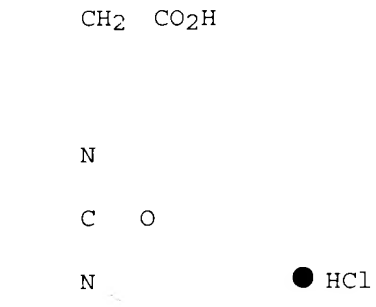
Absolute stereochemistry.

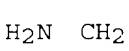


AN 1995:546553 CAPLUS
DN 122:290875
TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 32 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4234295	A1	19940414	DE 1992-4234295	19921012
	EP 592949	A2	19940420	EP 1993-116244	19931007
	EP 592949	A3	19940810		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2108093	AA	19940413	CA 1993-2108093	19931008
	JP 06199788	A2	19940719	JP 1993-252019	19931008
	FI 9304460	A	19940413	FI 1993-4460	19931011
	NO 9303647	A	19940413	NO 1993-3647	19931011
	NO 180232	B	19961202		
	NO 180232	C	19970312		
	AU 9348939	A1	19940428	AU 1993-48939	19931011
	AU 668765	B2	19960516		
	ZA 9307502	A	19950411	ZA 1993-7502	19931011
	CN 1087904	A	19940615	CN 1993-118925	19931012
	US 5442064	A	19950815	US 1993-135041	19931012
PRAI	DE 1992-4234295		19921012		

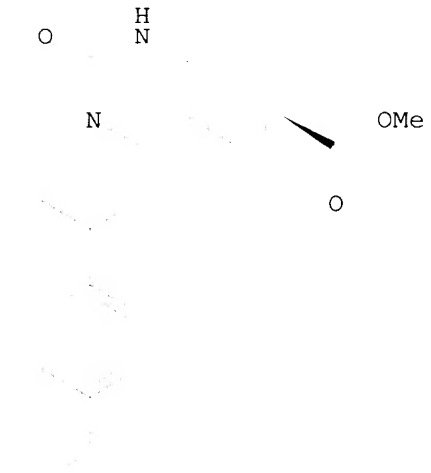
OS MARPAT 122:290875
AB ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene, etc.; D = CH2, CH2CH2, CO, CH2CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO2R5; R5 = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O2N)C6H4O2CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC50 of 4.300nM against platelet aggregation in vitro.
IT **162996-75-0P 162996-87-4P 162996-88-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as platelet aggregation inhibitors)
RN 162996-75-0 CAPLUS
CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

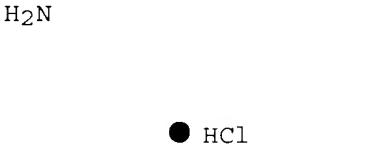




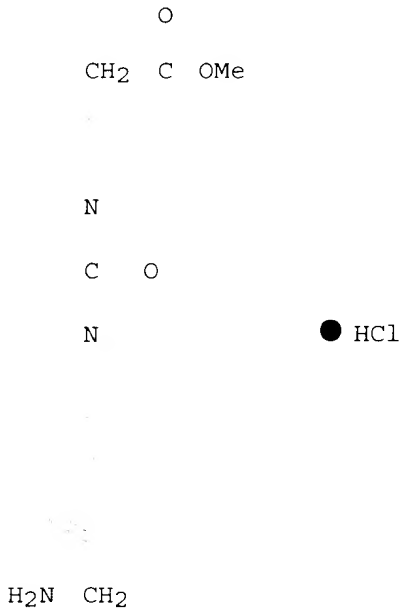
RN 162996-87-4 CAPLUS
CN Cyclohexanecarboxylic acid, 4-[[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]amino]-, methyl ester, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.





RN 162996-88-5 CAPLUS
CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



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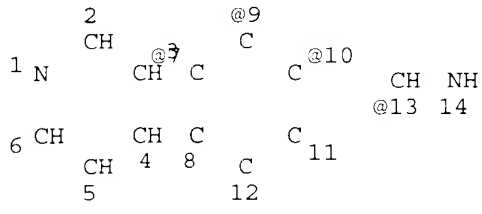
L2 STR



VPA 13-7/9/10 U
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 10 4
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

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SAMPLE SCREEN SEARCH COMPLETED - 9815 TO ITERATE

10.2% PROCESSED 1000 ITERATIONS 5 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 190370 TO 202230
PROJECTED ANSWERS: 561 TO 1401

L3 5 SEA SSS SAM L2

=> d scan

L3 5 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Piperidine, 4-[3-(aminomethyl)phenyl]-1-(2-bromo-4,5-dimethoxybenzoyl)-(9CI)
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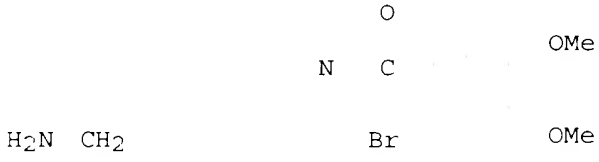
CI COM



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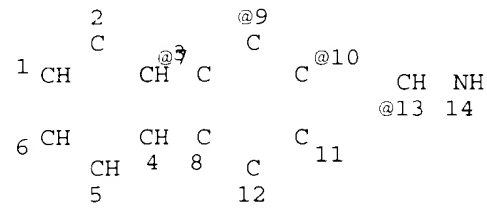

VPA 13-7/9/10 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 10 4
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 142.18 142.39

FILE 'CAPLUS' ENTERED AT 16:30:57 ON 04 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 4 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 3 Sep 2002 (20020903/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For

information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L5              8 L4
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L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090101	A1	20011129	WO 2001-US13811	20010427

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2000-12362 A 20000522
US 2001-843126 A 20010426
OS MARPAT 136:5917
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prepd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1999:348249 CAPLUS
DN 131:102177
TI Substituted piperidines - highly potent renin inhibitors due to induced fit adaptation of the active site
AU Vieira, Eric; Binggeli, Alfred; Breu, Volker; Bur, Daniel; Fischli, Walter; Guller, Rolf; Hirth, Georges; Marki, Hans Peter; Muller, Marcel; Oefner, Christian; Scalone, Michelangelo; Stadler, Heinz; Wilhelm, Maurice; Wostl, Wolfgang

CS Pharma Research Departments, F. Hoffmann-La Roche Ltd, Basel, CH-4070, Switz.
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(10), 1397-1402
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI

$O(CH_2)_3OCH_2Ph$ I

AB The identification, synthesis and activity of a novel class of piperidine renin inhibitors, e.g., I, is presented. The most active compds. show activities in the picomolar range and are among the most potent renin inhibitors ever identified.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1999:191411 CAPLUS
DN 130:242312
TI Pharmaceutical preparations containing piperidine derivatives as antimalarials
IN Bur, Daniel; Fischli, Walter; Matile, Hugues; Ridley, Robert George; Wostl, Wolfgang
PA F.Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9912532	A2	19990318	WO 1998-EP5570	19980902
	WO 9912532	A3	19990729		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9897409	A1	19990329	AU 1998-97409	19980902
PRAI	EP 1997-115510		19970908		
	WO 1998-EP5570		19980902		

AB Pharmaceutical prepns. contg. piperidine derivs. are used against chloroquine-sensitive and chloroquine-resistant pathogens and in the prodn. of corresponding medicaments; furthermore corresponding medicaments

and a method of treating malaria in a patient in need of such treatment comprises administering to said patient an effective amt. of a corresponding compd. or medicament. The IC50 of (3RS,4RS)-3-(naphthalen-2-ylmethoxy)-4-[4-(2-phenoxy-ethoxy)-phenyl]-piperidine (I) against chloroquine-resistant strains of Plasmodium falciparum was 0.6 .mu.M. A tablet contained I 500, lactose 149, PVP 15, dioctyl sodium sulfosuccinate 1, sodium carboxymethyl starch 30, and magnesium stearate 5 mg.

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1998:180759 CAPLUS
DN 128:243953
TI Preparation of N-aralkylpyridine-4-amines and analogs as thrombin inhibitors
IN Naylor-Olsen, Adel M.; Ponticello, Gerald S.; Vacca, Joseph P.; Hungate, Randall W.; Coburn, Craig; Phillips, Brian T.; Lewis, S. D.; Fraley, Mark E.
PA Merck & Co., Inc., USA; Naylor-Olsen, Adel M.; Ponticello, Gerald S.; Vacca, Joseph P.; Hungate, Randall W.; Coburn, Craig; Phillips, Brian T.; Lewis, S. D.; Fraley, Mark E.
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810763	A1	19980319	WO 1997-US15989	19970909
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	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744117	A1	19980402	AU 1997-44117	19970909
	AU 725403	B2	20001012		
	EP 927035	A1	19990707	EP 1997-942415	19970909
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001500864	T2	20010123	JP 1998-513809	19970909
PRAI	US 1996-26033P	P	19960913		
	GB 1996-24278	A	19961122		
	WO 1997-US15989	W	19970909		

OS MARPAT 128:243953
AB R1CHR2Z1Z2Z3R [I; R = 4-pyridyl, 4-amidino-1-piperazinyl, 4-aminopyridinium-1-yl, 6-amino- or amidino-3-pyridyl, C6H4[C(:NH)NH2]-4; R1,R2 = H, (hetero)aryl, (di)arylalkyl, CONH2, etc.; R1R2 = alkylene; Z1 = O, SO0-2, (alkyl)imino, etc.; Z2 = (un)substituted phenylene; Z3 = (CH2)m, (CH2)mNH, SO2NH, SO2(CH2)m, SO2, (CH2)mSO2; m = 1 or 2] were prepd. Thus, 4-(PhO)C6H4CO2H was amidated by 4-aminopyridine and the product reduced to give 4-(PhO)C6H4CH2NHR (R = 4-pyridyl). Data for biol. activity of I were given.

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1997:307688 CAPLUS
DN 126:277402
TI New 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes for treating heart and kidney insufficiency
IN Binggeli, Alfred; Breu, Volker; Bur, Daniel; Fischli, Walter; Gueller, Rolf; Hirth, Georges; Maerki, Hans-Peter; Mueller, Marcel; Oefner, Christian; Stadler, Heinz; Vieira, Eric; Wilhelm, Maurice; Wostl, Wolfgang
PA F. Hoffmann-La Roche Ag, Switz.
SO PCT Int. Appl., 492 pp.
CODEN: PIXXD2

DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9709311	A1	19970313	WO 1996-EP3803	19960829
	W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, TR				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2230931	AA	19970313	CA 1996-2230931	19960829
	AU 9667432	A1	19970327	AU 1996-67432	19960829
	AU 708616	B2	19990805		
	EP 863875	A1	19980916	EP 1996-927715	19960829
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1202152	A	19981216	CN 1996-197674	19960829
	JP 11500447	T2	19990112	JP 1996-510837	19960829
	BR 9610385	A	19990706	BR 1996-10385	19960829
	RU 2167865	C2	20010527	RU 1998-106388	19960829
	ZA 9607424	A	19970307	ZA 1996-7424	19960902
	NO 9800954	A	19980428	NO 1998-954	19980305
	US 6051712	A	20000418	US 1999-255185	19990222
	US 6150526	A	20001121	US 1999-456283	19991207
PRAI	CH 1995-2548	A	19950907		
	CH 1996-1876	A	19960726		
	WO 1996-EP3803	W	19960829		
	US 1996-711339	A3	19960906		
	US 1999-255185	A1	19990222		

OS MARPAT 126:277402
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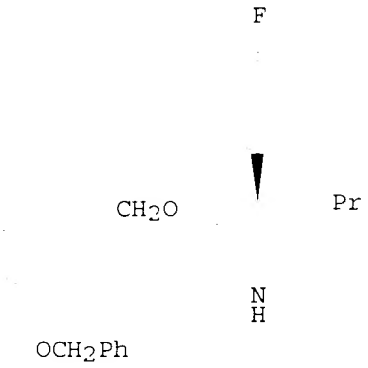


I

AB New piperidine and azabicyclooctane derivs. (> 1000 compds.) are renin inhibitors for treatment of high blood pressure, heart and kidney insufficiency. Thus, the piperidine deriv. I was prepd. from 1-benzyl-3-propyl-4-piperidinone by reaction with 4-FC6H4Br, followed by 1-benzyloxy-3-chloromethylnaphthalene and deblocking. I had a renin-inhibiting IC50 of 0.317 .mu.M.

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1995:546553 CAPLUS
DN 122:290875
TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian

PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 32 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

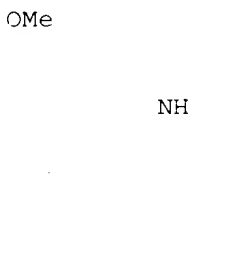
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4234295	A1	19940414	DE 1992-4234295	19921012
	EP 592949	A2	19940420	EP 1993-116244	19931007
	EP 592949	A3	19940810		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2108093	AA	19940413	CA 1993-2108093	19931008
	JP 06199788	A2	19940719	JP 1993-252019	19931008
	FI 9304460	A	19940413	FI 1993-4460	19931011
	NO 9303647	A	19940413	NO 1993-3647	19931011
	NO 180232	B	19961202		
	NO 180232	C	19970312		
	AU 9348939	A1	19940428	AU 1993-48939	19931011
	AU 668765	B2	19960516		
	ZA 9307502	A	19950411	ZA 1993-7502	19931011
	CN 1087904	A	19940615	CN 1993-118925	19931012
	US 5442064	A	19950815	US 1993-135041	19931012
PRAI	DE 1992-4234295		19921012		

OS MARPAT 122:290875
AB ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene, etc.; D = CH2, CH2CH2, CO, CH2CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO2R5; R5 = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O2N)C6H4O2CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC50 of 4.300nM against platelet aggregation in vitro.

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1994:533976 CAPLUS
DN 121:133976
TI Carboxylic Acid Derivatives and Their Uses as Pharmaceuticals
IN Himmelsbach, Frank; Linz, Guenter; Austel, Volkhard; Pieper, Helmut; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4241632	A1	19940616	DE 1992-4241632	19921210
	CA 2111035	AA	19940611	CA 1993-2111035	19931208
	EP 604800	A1	19940706	EP 1993-119786	19931208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	FI 9305513	A	19940611	FI 1993-5513	19931209
	NO 9304501	A	19940613	NO 1993-4501	19931209
	JP 06239817	A2	19940830	JP 1993-308419	19931209
	ZA 9309230	A	19950609	ZA 1993-9230	19931209
	AU 9352306	A1	19940623	AU 1993-52306	19931210
	CN 1094035	A	19941026	CN 1993-120876	19931210
PRAI	DE 1992-4241632		19921210		

OS MARPAT 121:133976
GI



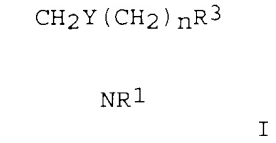
I

AB Pharmacol. active carboxylates were disclosed. A specifically claimed example compd., Me trans-4-[[4-(4-piperidinyl)phenyl]carbonylamino]cyclohexanepropanoate (I) was prepd. The claimed compds. are blood platelet aggregation inhibitors (antithrombotics).

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1992:235449 CAPLUS
DN 116:235449
TI Piperidine compounds, their preparation and use
IN Jakobsen, Palle; Kanstrup, Anders; Lundbeck, Jane Marie
PA Novo-Nordisk A/S, Den.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9201672	A1	19920206	WO 1991-DK206	19910715
	W: AU, CA, CS, FI, HU, JP, KR, NO, PL				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	IL 98757	A1	19970110	IL 1991-98757	19910708
	AU 9182241	A1	19920218	AU 1991-82241	19910715
	AU 661276	B2	19950720		
	EP 558487	A1	19930908	EP 1991-913359	19910715
	EP 558487	B1	19981007		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06500076	T2	19940106	JP 1991-512512	19910715
	AT 171943	E	19981015	AT 1991-913359	19910715
	CN 1058207	A	19920129	CN 1991-104954	19910718
	ZA 9105647	A	19920527	ZA 1991-5647	19910718
	NO 9300143	A	19930118	NO 1993-143	19930115
	NO 179974	B	19961014		
	NO 179974	C	19970122		
	US 5328917	A	19940712	US 1993-65513	19930520
PRAI	DK 1990-1724		19900718		
	DK 1991-117		19910124		
	US 1991-728930		19910712		
	WO 1991-DK206		19910715		

OS MARPAT 116:235449
GI



AB Title compds. I (R1 = H, C1-8 alkyl, C1-8 alkyl, C1-8-alkoxy-C1-8-alkyl, C3-8 cycloalkyl, C2-6 alkenyl, C4-8 cycloalkylalkyl, Ac, C2-6 alkynyl; R3 = 3,4-methylenedioxyphenyl, (substituted) Ph naphthyl, (substituted) 5-, 6-membered heterocyclyl contg. 1 or 2 N, O, S X = H2N, O2N, mono-, dialkylamino, HO2C, alkanoylamino, etc.; Y = O, S, RN whereas R = H, C1-5 alkyl; n = 0-4) or a salt thereof, useful in treatment of Ca overload, are prepd. 3-[(Benzenesulfonyloxy)methyl]-1-butyl-4-phenylpiperidine was mixed with 4-(MeO)C6H4CH2NH2 and heated for 4 h at 90.degree. to give I (R1 = Bu, R3 = 4-(MeO)C6H4, X = H, Y = HN, n = 1) (II). II showed an inhibition of Ca uptake in brain synaptosomes, IC50 of 2.7 .mu.g/mL, vs. diltiazem 96 .mu.g/mL. A tablet formulation comprising I is given.

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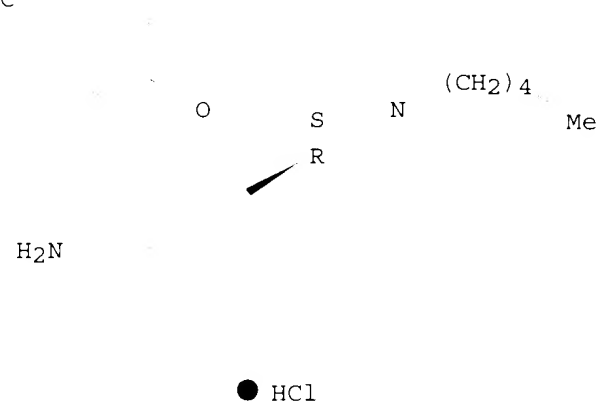
L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
IT **141360-48-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as calcium antagonist)
RN 141360-48-7 CAPLUS
CN Benzenemethanamine, 4-[1-pentyl-3-[[4-(trifluoromethyl)phenoxy]methyl]-4-piperidinyl]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



AN 2000:243073 CAPLUS
DN 132:246060
TI Effects of fluticasone propionate on tryptase serum levels in allergic rhinitis
AU Bruno, G.; Andreozzi, P.; Magrini, L.; Zaino, S.; Graf, U.
CS Istituto di I Clinica Medica, Fondazione A. Cesalpino Universita La Sapienza, Rome, Italy
SO World Congress of Asthma, 16th, Buenos Aires, Argentina, Oct. 17-20, 1999 (1999), 121-124. Editor(s): Neffen, Hugo E.; Baena-Cagnani, Carlos E.; Yanez, Anahi. Publisher: Monduzzi Editore, Bologna, Italy. CODEN: 68UFA9
DT Conference
LA English
AB In allergic rhinitis (AR) such as in other allergic reactions, studies draw attention to the potential of neutral proteases, proteoglycans, eicosanoids and various cytokines that are released by mast cells. Among these mediators, **tryptase** is known to be a specific marker of mast cell activation. This study was devoted to evaluate the serum **tryptase** in AR and the effect of fluticasone propionate (Ftp) on serum levels of this mediator. The basal values of **tryptase** (M.+-.SD: 6.1.+-.2.4 .mu.g/L) resulted to be significantly ($p < 0.02$) higher in 13 AR subjects than in the controls (3.0.+-.1.2 .mu.g/L). **Tryptase** values decreased significantly ($p < 0.04$) after 15 days of 100 .mu.g of Ftp treatment (M.+-.SD: 4.5.+-.3.1.mu.g/L) which was administered twice a day. After two weeks of wash-out, **tryptase** values (M.+-.SD: 5.5.+-.2.6 .mu.g/L) increased again significantly ($p < 0.05$). The intranasal **corticosteroids** are effective in modulating the mucosal inflammation of AR, leading also to a decrease of mast cell activation.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT